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NZC Chemistry
IN NEW ZEALAND

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Focus on Nutrition, Pharmaceuticals, Cosmetics, Microbiology

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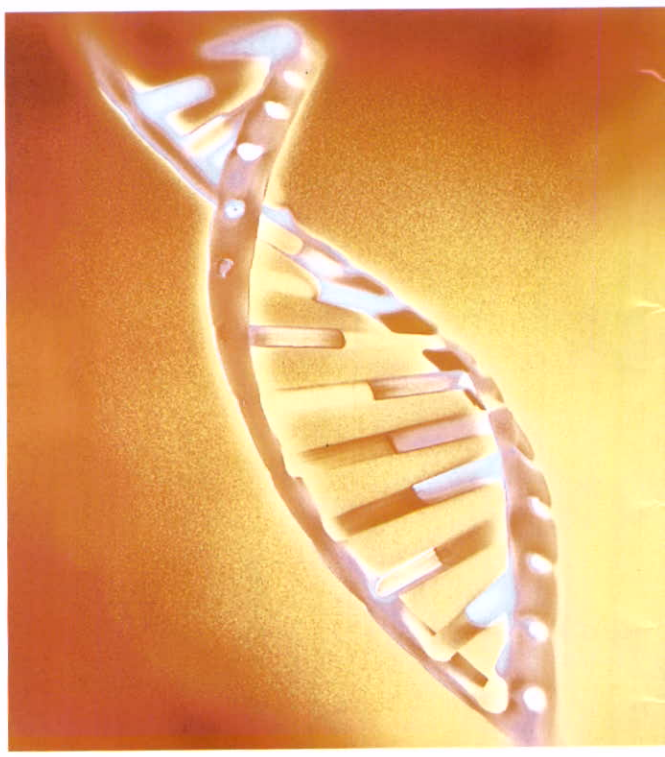

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COVER STORY

Compact Spectrum One FT-IR Systems From Perkin-Elmer Signify A New Generation Of Sophisticated, User-Friendly Technology

Touch screens, atmospheric correction, and question/answer wizards are just some of the features that make the new, compact Spectrum One™ Fourier-Transform Infrared (FT-IR) systems from Perkin-Elmer a major advancement in flexible, user-friendly technology. Based on proven Spectrum™ FT-IR technology, the new Spectrum One systems work harder using smarter accessories, easier software and faster data collection, which allows inexperienced users to spend less time learning to optimise components, parameters and data. Flexible enough to fit a wide variety of applications, Spectrum One systems are also simple enough to run after minimal training due to built-in touch screens, which can be programmed in the local language.

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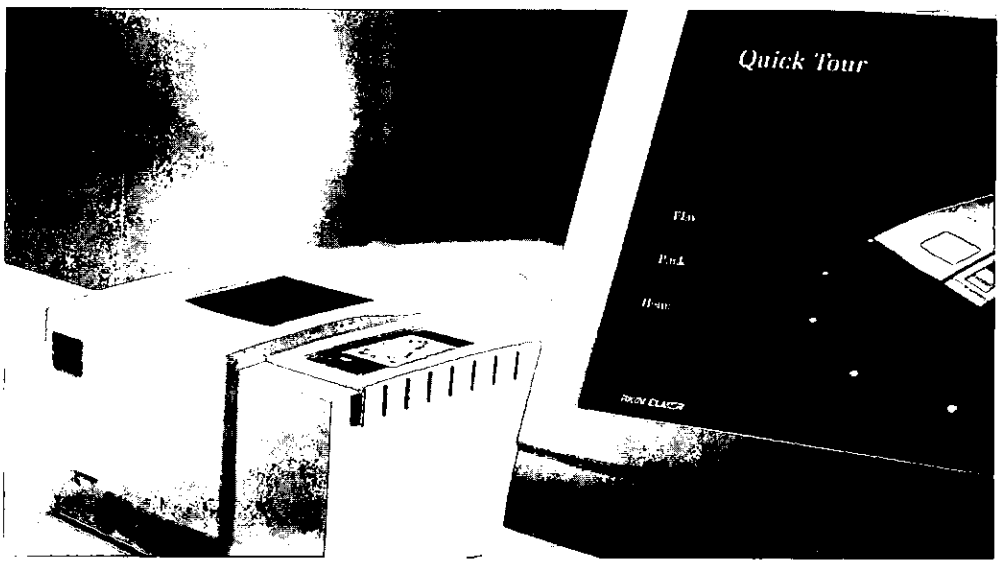

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IN NEW ZEALAND

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Deadline for material *5th of the month of publication*

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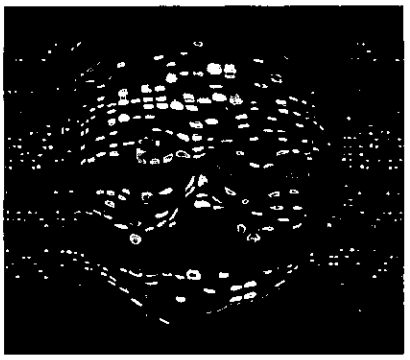
NZ Science Scene

PE Biosystems Relocates Head Office



PE Biosystems has relocated its head office in Melbourne to:
52 Rocco Drive, Scoresby
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Please note that the NZ toll free customer numbers have not changed:
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If you have any enquiries please do not hesitate to contact your New Zealand representative Stacey Nelson.

Email: nelsonse@pebio.com

Recommendation To Government By IBAC

Last month, the Independent Biotechnology Advisory Council (IBAC) issued a statement advising Government to delay the consideration of the unrestricted release of genetically modified (GM) plants.

IBAC has written to the Minister of Research, Science & Technology, Hon. Maurice Williamson, recommending that any decision about the first release of GM plants should await the findings of IBAC's public consultation which is currently taking place.

In a letter to the Minister, IBAC Convener, Professor Peter Gluckman, says that to the Council's knowledge there has been no detailed analysis of the economic, trade or other implications of New Zealand releasing GM plants on a commercial scale.

He said while the Environmental Risk Management Authority (ERMA) had considered and approved a number of applications for contained laboratory development or contained field testing of GM plants it had not received any applications yet requesting the release of GM plants in an unrestricted manner.

"Any decision to release genetically modified plants needs careful consideration as, unlike the field testing situation, the Hazardous Substances and New Organisms (HSNO) Act provides ERMA with no legislative power to place any degree of control on released GM plants.

The proposition has been advanced that there may be advantages to New Zealand in being able to market produce grown in a GM plant free environment. Thus the unrestricted release of GM plants might affect a specific niche element in our agricultural sector. The release of such plants may also affect our 'clean green' image as a nation," he says.

IBAC, which last week released its public consultation booklet "The Biotechnology Question" was established by Government in May to help the New Zealand public explore and consider biotechnology issues.

It aims to stimulate dialogue and enhance public understanding of biotechnology and will also provide independent advice to Government on the environmental, economic, ethical, social, and health aspects of biotechnology.

Professor Gluckman said IBAC's consultation with the public had only

just begun and the Council believed the consultation process should take its course before an irrevocable decision such as the unrestricted release of GM plants was made.

"We believe that there is a need to identify and investigate the broader economic, social and philosophical issues before any decisions are made."

"It is important to note that this recommendation is limited only to the unrestricted release of GM plants and does not affect ERMA's continued approval of the contained development of GMO's or controlled field testing," he said.

IBAC began its first round of public consultations in Wellington in September.

"The Biotechnology Question", which is free to the public, is available through public libraries and Citizens' Advice Bureaux. It can also be ordered by sending postal details to info@ibac.org.nz or, for those without email access, by phoning the toll free number 0800 50IBAC or 0800 504222."

The Hon. Maurice Williamson (Minister of Research, Science and Technology) and Hon. Simon Upton (Minister of the Environment) issued statements in support of IBAC's recommendations. The Ministers' statements can be read on the Government News Release Archive at http://admin.executive.govt.nz/cgi-bin/ExecutivesDisplay?type=press&location=central

Sir Ian Axford To Receive Honorary Doctorate

Sir Ian Axford FRS, Honorary FRSNZ, one of New Zealand's most distinguished scientists, received an honorary Doctor of Science degree from Victoria University recently at a special ceremony held as part of the University's centennial celebrations.

For Sir Ian it is the latest in a long list of honours, including being named "New Zealander of the Year" for 1995 and having a knighthood conferred by Queen Elizabeth II the following year. He was made an honorary Fellow of the Royal Society of New Zealand in 1993. In 1994 the Royal Society awarded him the country's top science award, the Science and Technology Gold Medal.

His former positions include those of Vice-Chancellor of Victoria University (1982-85), Chairman of the Foundation for Research, Science and Technology (July 1992-October 1995), and Chairman of the Marsden Fund for basic research (December 1995 - December 1998). He remains a Director of the Max-Planck Institut fur Aeronomie in Germany, a position he has held since 1974.

NZVCC To Administer New Scholarships

Increased public awareness of the oil and gas exploration industry is the purpose behind the establishment of the Petroleum Exploration Association Scholarship for Excellence in Earth Science. One scholarship, worth up to $5000 per annum will be awarded each year. The term of each award will be two years followed by a review to determine continuation.

Candidates will need to be embarking on a masters degree and demonstrate a high level of academic achievement and the relevance of their chosen topic to the exploration industry. Their research/study will need to be undertaken in geology, hydrocarbon geochemistry or geophysics.

Massey University Emeritus Professors Dick and Mary Earle have established the Dick and Mary Earle Scholarship in Technology to support and encourage postgraduate research into aspects of technology in New Zealand universities.

The specific purpose for the scholarship is to provide funds for individuals to study at masterate or PhD levels at a New Zealand university or research institution in one or both of two fields: innovation and product development, and bioprocess technology.

The value of the scholarship in technology will be $15,000 per annum. The scholarship is available for three years according to the course of study. Subject to the availability of finance, there will be up to six scholarships at any one time. One scholarship will normally be offered annually in each of the two designate fields.

For further information about these scholarships see:
http://www.nzvcc.ac.nz

Statistics Show Progress Towards Bright Future

New Zealand's future as a "knowledge society" has been in the headlines lately with the high-profile launch of the Bright Future initiatives. But what are the latest statistics saying about our progress towards a knowledge society?

The 1998/99 Research and Experimental Development Statistics released by MoRST in August show solid overall growth in Research and Development (R&D) expenditure with some spectacular growth in business R&D.

The figures show New Zealand's R&D expenditure by the Government, business and university sectors during 1997/98.

New Zealand's total R&D reached a record high in 1997/98, at an estimated $1107.4 million, equivalent to 1.1 percent of Gross Domestic Product (GDP).

New Zealand has one of the highest R&D growth rates in the Organisation for Economic Cooperation and Development (OECD). Total R&D expenditure increased on average at 6.2 percent per year from 1990/91 to 1997/98.

Government Investment
Within Government, R&D funding reached $561.8 million in 1997/98, equivalent to 0.57 percent of GDP. Government funds continue to be a major source of R&D financing, accounting for 54 percent of the total R&D investment in New Zealand. Health was the largest output area of Government funding in 1997/98, followed by horticultural, arable, food and beverages and the society and cultural area.

Staff employed in the Government R&D sector comprised 3816 Full Time Equivalents (FTE) in 1997/98. Researchers represented 46.3 percent, technicians 31.7 percent and support staff 22 percent. Crown Research Institutes (CRIs) comprised 88 percent of R&D staff in the Government sector in 1997/98, compared to 91 percent in 1995/96.

Nationally, R&D staff continue to rise steadily to a total of 12,899 in 1997/98. Of the total, 7904 (61.2 percent) were male and 4995 (38.8) percent were female.

Business Performance
Total Business Expenditure on R&D (BERD) was $312.5 million in 1997/98, an increase of 30 percent to 0.32 percent of GDP. This is a record level for business R&D since the R&D surveys began in 1990/91.

Since 1990, the business sector has shown a shift in its R&D emphasis. More R&D is being performed by the industries producing communications and electronic equipment and instruments. R&D in the service sector has also increased including e-commerce and software research.

The proportion of business R&D in the high tech manufacturing sector jumped 10.4 percentage points from 1995/96 to 1997/98.

University R&D
Within New Zealand's universities R&D expenditure was estimated at $403.5 million in 1997/98, equivalent to 0.4 percent of GDP. This expenditure is relatively high in international terms. The major source of R&D funds is Government (60 percent), followed by universities' own funds including student fees and other income (28.7 percent).

Universities have the highest proportion of FTE researchers compared with the business and government sectors. The full report can be read at:
http://www.morst.govt.nz

Citation Received By Chemist

Emeritus Professor James Duncan FRSNZ, formerly of Victoria University of Wellington, has just received a Citation of Excellence for his paper on "The Chemistry of Social Interactions" in *Technological Forecasting and Social Change*, 1999, Vol. **60**, No 2. by ANBAR Electronic Intelligence. The Highest Quality Rating was awarded by ANBAR to this paper from a database of no less than 90,000 pieces from over 400 of the world's top management journals. It has been placed in their "Hall of Fame".

Although this paper applies chemical theory to the social sciences, the award was made, to the astonishment of the author, by an organisation handling professional journals in management.

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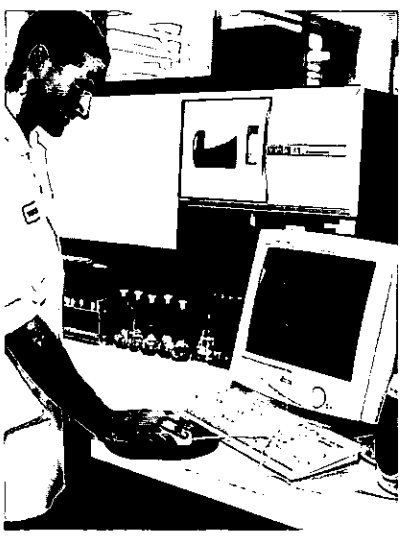
Efficient New Laboratory Opens In Napier

A new $2.2 million laboratory near Napier will provide primary industry throughout New Zealand with fast, low-cost and high quality agronomic analysis.

"Analytical Research Laboratory (ARL) features state-of-the-art technology and will be able to analyse up to 40,000 soil and plant tissue samples from around the country each year," says Ravensdown Chairman Jim Pringle.

The laboratory, which was officially opend by Hon. Simon Upton (Minister of Crown Research Institutes) on 29 September, is a joint venture between Ravensdown and AgResearch.



ARL's new Varian ICP which can operate unstaffed and can analyse for five to six cations on more than 200 soil samples overnight.

"The investment by both parties in ARL will establish the laboratory as a national, high volume, high accuracy and low-cost agronomic laboratory," says Mr Pringle.

ARL chairman and AgResearch chief executive officer Keith Steele says ARL combines state-of-the-art equipment with the most advanced analytical techniques to help farmers increase their profitability and optimise their outputs by ensuring their practices are sustainable for the long term benefit of the environment.

The new purpose-built $2.2 million Analytical Research Laboratory near Napier

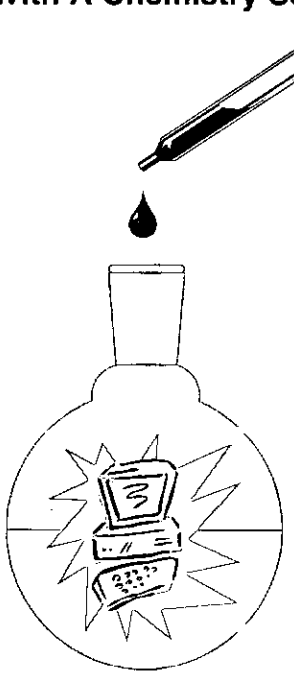
Dr Steele says it's a complete package designed to keep the cost of analyses down. "The sophisticated approach offered by ARL will support responsible farming in a world which is beoming more environmentally conscious. The combination of soil, plant and food analysis with environmental testing provides the opportunity for integrated solutions," Dr Steele says. "The ability to provide integrated solutions is an important competitive advantage for our industries which New Zealand must preserve."

"The relationship between AgResearch and Ravensdown is seen by both parties as a natural partnership" says Mr Pringle.

Each year New Zealand farmers spend six hundred million dollars on fertiliser and as a 100 percent New Zealand farmer owned co-operative, Ravensdown wants to help farmers make the most of this substantial investment. AgResearch provides the hard scientific research and Ravensdown provides the application of that science. Our involvement in the laboratory enables Ravensdown to provide a complete package of soil products, sales and service," says Mr Pringle.

Research Frontiers

Making Computers With A Chemistry Set



"We can potentially get the computational power of 100 workstations on the size of a grain of sand", claims James Heath, Professor of Chemistry at UCLA (University of California, Los Angeles, USA). He and a team of researchers from UCLA, together with researchers from Hewlett-Packard Labs in Palo Alto, California, recently devised a way to build computer circuitry using logic gates made from organic molecules rather than silicon (*Science*, 1999, **285**, 391).

A chemical computer chip is one of the holy grails of computing, offering the potential for faster, smaller and more efficient computers. "You can potentially do approximately 100,000 million times better than a current Pentium in terms of the energy required to do a calculation" says Heath. "I believe we can improve energy efficiency by at least six or seven orders of magnitude ... [and] move into a realm that silicon could never achieve".

Today's computer technology, which uses silicon-based computer chips, is also rapidly approaching the upper limits of its capability. Physical and cost constraints are beginning to place boundaries on just how many transistors can be crammed onto a computer processor. In a recent letter in *Nature* (1999, **399**, 729), researchers from Bell Laboratories in New Jersey, USA, predicted that silicon-based computer chips will reach their physical limit by 2012, constrained by the fact that a layer of silicon dioxide used as an insulator on the chips must be at least four to five atoms thick. Chips created using organic chemicals rather than silicon offer a possible solution to this size problem.

Chemical computers are not without their own problems, however. Any chemically-prepared system will need to be able to tolerate defects in its architecture as a result of finite chemical reaction yields. Current computers are basically defect-free.

Heath and his team theorised that one way around this problem would be to lay down millions of wires and switches - some defective, some not - in a simple grid, and then electronically configure the grid into proper circuits, by-passing any defective sections.

This approach has already been shown to work with current computer technology. Within the past few years a working supercomputer named Teramac has been constructed by researchers at Hewlett-Packard using a large number of partially defective components linked together by software routines that are able to work around the defects. What Heath and his team of researchers have now achieved is the first step in creating a chemical version of this kind of computer.

Using a class of chemical compound known as a rotaxane, the researchers joined microscopic perpendicular wires together to form a grid of molecular switches. Rotaxanes consist of a dumb-bell-shaped component encircled by ring-shaped components. In this instance the dumb-bell-shaped component contained two bipyridinium units, while the encircling rings were bis-*para*-phenylene-34-crown-10.

The presence of the rotaxane linkage allowed a current to flow from the bottom wire to the top wire, turning the switch 'on'. But, if the rotaxane linkage was oxidised by applying a small positive voltage between the perpendicular wires, current could no longer flow, turning the switch 'off'. By joining these switches together, and turning certain ones off or on, the researchers were able to fabricate simple logic gates (AND and OR).

This is only a first step and further problems remain. The wires used by the team were far larger than those used in current computer chips (11 μm wide as opposed to 250 nm), although Heath says that there is no reason why carbon nanotubes could not eventually be used. In addition, once the rotaxane linkage has been oxidised the switch is turned off for good, which means that this technique cannot be used to create a writeable memory source. However, the researchers are currently investigating similar organic molecules in the hope of finding one that can switch back and forth repeatedly.

Nevertheless, Heath predicts that prototypes of hybrid computers using both conventional and chemical techniques are only a few years away. "What once seemed like science fiction is now looking more and more like actual science", he says.

Research Frontiers

A Cat Fight Against Aids

By studying a version of the Aids virus that infects cats - feline immunodeficiency virus (FIV) - researchers at the Scripps Research Institute in La Jolla, California, USA, have developed a new form of protease inhibitor, which is effective against current drug-resistant strains of the human virus (*J. Am. Chem. Soc.* 1999, **121**, 1145).

Protease inhibitors are the cornerstone of modern Aids therapy and they work by disabling proteins that the virus needs in order for it to multiply. HIV can, however, quickly mutate to become resistant to these inhibitors.

The researchers discovered that current protease inhibitors have binding sites (P3 residues) formed from large chemical structures, but that the respective binding sites, (S3 subsites) on the protease of resistant strains of HIV are reduced in size, so the inhibitors are no longer able to attach themselves.

Using FIV as their model, because its protease naturally has small binding sites, the researchers developed a new class of inhibitors with smaller structures at the relevant binding sites. In tests, the new class of inhibitor was effective against HIV protease and the drug-resistant mutants. It may also become the first treatment for feline Aids, which is a significant threat to the world cat population.

A Vitamin C Boost May Help Relieve Stress

Consuming very large amounts of vitamin C may be an effective method of relieving stress, according to P Samuel Campbell and his co-workers at the University of Alabama, USA. Announcing the group's findings at the ACS meeting in New Orleans in August, Campbell said that he had observed significant reductions in the level of stress hormones in rats fed on 'megadoses' of the vitamin. The group's findings are a boost for advocates of the controversial theory that megadoses (much higher than the recommended daily allowance, or RDA) of vitamin C are beneficial in preventing a wide range of illnesses, including cancer and heart disease. They may also go some way towards explaining earlier studies, which have shown improved immune function in elderly women and a reduced incidence of stress-related respiratory infections in marathon runners fed megadoses of vitamin C.

The Alabama researchers made their discovery on 'stressed' rats (which had been immobilised in a wire mesh cage for one hour a day over a period of three weeks). The animals were fed 200 mg of vitamin C per day - the equivalent of several grams a day for humans, a dose that far exceeds the 60 mg RDA. Rats that were stressed and not fed vitamin C had almost three times the level of the glucocorticoid hormone corticosterone seen in the control rats. Vitamin C also effectively alleviated other common stress symptoms in these rats, such as loss in body weight, reduction in size of the thymus gland and spleen, and enlargement of the adrenal glands.

In addition, the treatment increased levels of natural IgG antibodies circulating in the blood by about a fifth, thereby raising the body's defence mechanism against illness. Interestingly, vitamin C raised IgG levels slightly higher in the control group of rats that were not subjected to stress than in the stressed rats, perhaps suggesting that stressed individuals need higher doses of vitamin C to maintain good health.

Paradoxically, Campbell proposes that the effects of vitamin C may be the result of a 'negative feedback loop' acting to reduce levels of vitamin C already stored in large quantities in the adrenal gland. The adrenal gland's regulatory hormone ACTH promotes the secretion of glucocorticoids (cortisol in humans) from the adrenal gland that trigger the body's 'fight or flight' response in times of stress. These hormones also suppress the immune system, which partly explains the link between stress and susceptibility to illness. Although the role of vitamin C in the adrenal glands is unclear, ACTH secretion depletes levels of the vitamin in a dose-dependent fashion, which implies that endogenous vitamin C supports the production of stress hormones. Campbell suggests that large quantities of vitamin C in the diet may mediate its effects by inhibiting the production and use of this endogenous vitamin C to decrease hormone secretion. The group's findings should make us take a much sharper look at the RDA level of the

vitamin, particularly for individuals suffering from chronic stress, he says.

Eating Chocolate Is Not All Bad!

We should 'not feel too guilty about eating chocolate' was the consensus of opinion among a number of scientists presenting their work at the American Chemical Society meeting in California earlier this year.

Joe Vinson and his group at the University of Scranton, Pennsylvania, USA, reported their recent findings that cocoa and chocolate contain more polyphenol antioxidants - a group of compounds that are associated with a decreased risk of cardiovascular disease - than any of the vegetables, fruits and beverages that they investigated. "One dark chocolate bar (40 g) contains roughly twice the amount of polyphenols as the average daily serving of fruits and vegetables in the American diet," confirmed Vinson.

Harold Schmitz, Group Research Manager for Analytical and Applied Sciences at Mars, New Jersey, was also upbeat. Chocolate, he said, contains a great diversity of a class of polyphenols called flavonoids - specifically procyanidins and oligomeric procyanidins. Mars researchers, in collaboration with scientists at the University of California Davis, carried out *in vitro* studies of the individual flavonoids revealing that the flavonoids significantly inhibit LDL cholesterol oxidation, a process that is thought to be one of the key initial events associated with the buildup of plaque in the arteries.

Naomi Osakabe, a researcher at the Functional Foods Research Laboratories, Saitama, Japan, said that one of the ingredients of chocolate and cocoa - cacao liquor - also contains major antioxidants, specifically epicatechin, catechin, clovamide, quercetin, and their glucosides. These showed physiological effects in experimental animal models, including anti-ulceratic activity in rats and tumour production inhibition in mouse skin, she said.

Although further work needs to be done to see if the effects of the high antioxidant levels translate to humans, the overall consensus of the researchers was summed up by Schmitz: "if you like chocolate, don't feel too bad about eating it - it fits right in with a well-balanced diet".

However, the researchers were careful to point out that they were not advocating that people eat a lot of chocolate. "Remember, chocolate has a high fat and sugar content," said Vinson.

Chemistry May Lead To Earlier Detection Of Cancer

New imaging agents that seek out cancer cells could eventually lead to earlier tumour detection and so improve the prognosis in various cancers.

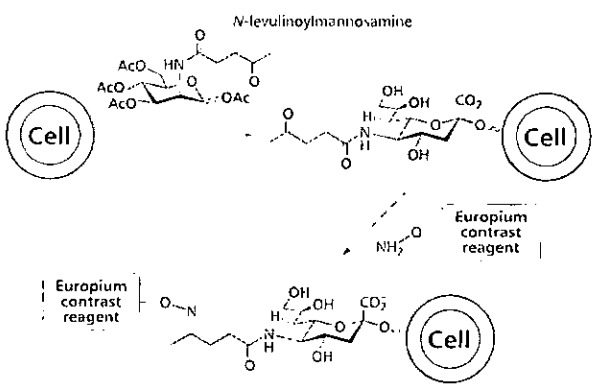
Carolyn Bertozzi and her colleagues at the University of California, Berkeley, USA, have found that they can target cells with a magnetic resonance imaging (MRI) contrast agent by exploiting differences in cell surface antigens without the need to resort to often poorly-specific antibodies.

Bertozzi reasoned that she could use subtle differences in the way in which healthy and tumour cells metabolise carbohydrates expressed on their surfaces. Tumour cells exhibit abnormal surface carbohydrates that are normally only expressed during foetal development. In many cancers - gastric, colon, pancreatic, liver, lung, prostate and breast cancer, as well as in leukaemia - these abnormal carbohydrate structures contain the monosaccharide sialic acid, which raises levels of this sugar on tumour cell surfaces.

Because healthy cells produce far fewer sialosides, their abundance might be used to distinguish tumour cells from normal cells. This difference could be used to target MRI contrast agents, which enhance cancer tissue images.

The researchers knew that the enzymes that produce sialosides can tolerate non-natural substrates well. They reasoned that, by using a compound such as *N*-levulinoylmannosamine as the substrate, they could produce sialosides on a tumour cell with a ketone group that would act as a unique chemical handle for contrast reagents bearing an amino-oxy or hydrazide side-chain. The ketone should thus enhance tumour imaging.

The team synthesised an amino-oxy derivatised contrast reagent, (GdDTPA), and swapped the gadolinium ion for a fluorescent europium ion so that they could detect its presence on cells.



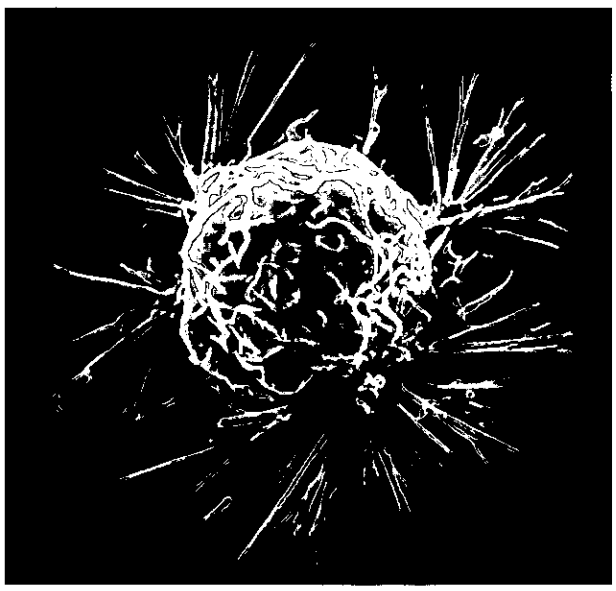
To test their idea, they cultured human T-cell lymphoma cells with *N*-levulinoylmannosamine as feed-stock. Because lymphoma cells are heavily sialylated, their ketone expression should be high.

The researchers then added the Eu-based contrast reagent and measured fluorescence levels to see how well the agent bonded to the cancer cells. For control purposes, they also

made measurements without the amino-oxy modification. The team found that tumour cell targeting depended strongly on the presence of the ketone on the cell surface and the reactive amino-oxy group on the contrast agent.

"We are only at the very early stages", Bertozzi says, "but we are doing some *in vitro* MRI work to establish the parameters of our reagent and depending on the outcome of these studies we might want to design second-generation analogues with enhanced relaxivity for later *in vivo* experiments."

Novel Chemotherapy Drug Activated With Light



Scanning Electron Micrograph of a spreading breast cancer cell.

Chemotherapy may become less of an ordeal for cancer sufferers as a result of research carried out by a team of European chemists. The team, led by Professor Peter Sadler from the University of Edinburgh, Scotland, has developed a new version of cisplatin (*cis*-$[PtCl_2(NH_3)_2]$), an important anti-cancer drug used in chemotherapy. The new, more flexible and more effective version can be specifically targeted on cancer cells, because it only becomes active one it has been triggered by light shone onto it through a fibre optic cable (*Angew. Chem. Int. Ed.*, 1999, **38 (10)**, 1460).

Cisplatin works by binding to a cancer cell's DNA, thereby preventing DNA replication in dividing cells. However, the action of cisplatin is not restricted to cancer cells: the drug also attacks healthy cells. The unwanted side effects of chemotherapy, such as hair loss and nausea, are a result of cytotoxic (cell destroying) drugs attacking all the fast-growing cells in the body.

The idea of using light to target tumour cells specifically is not new. In photodynamic theory, light is used to activate compounds such as porphyrins, so that they only become cytotoxic at the irradiated site (*Chem. Br.*, May 1998, p 18 and p 45). Research has already shown that the anti-cancer effects of cisplatin can be similarly triggered by irradiating iodine-containing platinum precursors of the drug with light (N A Kratochwil *et al., J. Med. Chem.*, 1996, **39**, 2499).

Now Sadler's team has developed a new type of iodine-containing cisplatin prodrug, which is activated by visible light to form a cisplatin-like compound. This new compound has the potential to become a more effective anti-cancer agent than cisplatin itself. Like cisplatin, the new agent binds to a cell's DNA (in this study the nucleotide guanosine 5′-monophosphate (5′-GMP), but unlike cisplatin it is able to bind to two separate nucleotides, thus making it much more difficult for the cancer cell to mount a defence. Furthermore, Sadler and his team have also found a potential way to control the activity of the agent, by altering the axial ligands of the platinum precursor and thereby controlling the photoreaction rate.

There are still problems to be overcome: at the moment, the type of precursor platinum complex Sadler and his team are using is so reactive that it would damage healthy cells. However, Sadler hopes that by making small changes to the design of the complex, he can reduce its chemical reactivity, while retaining its ability to photoreact to produce a very effective anti-cancer agent.

Pilot Internship Project With Udine University, Italy

The University of Udine plans to organise a 3-6 month internship programme for its graduate students in foreign institutions. In turn, the University of Udine offers free meals and accommodation at their student house and free attendance at University courses for the period of the internship.

Members of the NZIC are invited to contact Francesca Giorgetti directly if they are interested.

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INFLUENZA: INCONVENIENCE OR KILLER VIRUS?

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To most of us influenza is no more than an inconvenience. We may get a dose of the 'flu' during the winter months, resulting in a couple of days off work, then life continues as before. However, to the very young, elderly or sick, or when a particularly virulent strain appears, influenza can be a killer.

Influenza and Its Symptoms

Influenza is a disease of the respiratory tract. It generally strikes in the autumn and winter months, although large numbers of cases have been documented outside of this period during serious pandemics.[1] It has an incubation period of 1–3 days and duration of 2-3 days. Common symptoms include chills, fever, headache, sensitivity to light, sore muscles, backache, weakness and fatigue.[3] The majority of these symptoms last for only a few days but, depending on the severity of the case, fatigue may persevere for up to two weeks. Secondary bacterial infections, usually pneumonia or bronchitis, are often observed and have proved fatal, especially at the time before antibiotics were readily available. Unlike measles, mumps and smallpox, influenza remains an uncontrolled disease – there are approximately 350 million cases worldwide each year, and currently influenza still kills more Americans each year than AIDS.

The name 'influenza' was first used by the Italians during the 1504 epidemic.[1] It was adopted by the English during the 1743 epidemic and has been in use ever since. It was once thought that the disease was caused by the alignment of the stars and planets. Thomas Willis wrote, of the 1658 epidemic, "*About the end of April, suddenly a Distemper arose, as if sent by some blast from the stars.*"[2] In 1806, Robert Johnson postulated that the disease was propagated by a form of 'contagion', but the editor of the publication disagreed, adding a footnote to the view that influenza was "*exclusively of atmospheric origin...possibly a deleterious gas.*"[2]

In 1931 Dr Richard Shope, from the Rockefeller Institute for Comparative Pathology at Princeton, New Jersey, isolated an influenza virus from pigs and, by cross-infection experiments, showed it to be the causative agent.[1] Dr Christopher Andrewes and co-workers, from the National Institute for Medical Research, London, achieved the first isolation of a human influenza virus in 1933.† But even today the exact cause of the disease remains a matter of some debate. Although the existence of the virus is undisputed, direct person-to-person transmission does not account for the seasonality of the disease.[2]

The Virus

Influenza viruses are members of the *orthomyxoviradae* family of enveloped viruses. They have two major surface glycoproteins, neuraminidase (or sialidase) and haemagglutinin, which protrude like spikes from the viral membrane. Genetic material is stored in eight short lengths of RNA, each of which codes for a different viral protein.[1]

There are three types of influenza virus, A, B, and C. Type B is responsible for mild forms of the disease and is only observed in humans. Type A also affects other animals and is responsible for all serious outbreaks of the disease. Type A viruses can be classified into many subtypes according to surface proteins (see later).[1,3] Type C influenza comes from a different class of viruses that won't be discussed in this article.

Influenza viruses undergo constant and rapid mutation,‡ which reduces the effectiveness of the immune system and makes pharmaceutical development very difficult. These mutations occur by two distinct methods:

Antigenic "drift" occurs in both influenza A and B. It is caused by point mutations in the antigenic regions of the surface glycoproteins, which result from the high error rates of influenza RNA polymerase. The induced changes, although small, are significant enough to present a new and unrecognised antigen to the human immune system.

Antigenic "shift" is only observed in influenza A viruses and results from a re-assortment of the viral genome. This is believed to occur when a single animal, often a pig or bird, becomes simultaneously infected with two different strains. During the packaging of RNA into the viral particles, segments of RNA encoding for surface glycoproteins may be swapped between the two strains giving a new virus, which appears completely different in the eyes of the immune system.

Surface Proteins

In order to understand the virus and current attempts at combating the disease it is necessary to take a closer look at the two important surface glycoproteins.

Haemagglutinin has a molecular mass of approximately 225 kilodaltons. In its native form it occurs as a trimer with the overall structure of a spike sticking out from the viral membrane. Each monomer consists of two polypeptides: HA_1 forms the membrane distal globular

† Andrewes went on to become the first director of the World Health Organisation's influenza unit.

‡ Prior to HIV, influenza was the most variable known virus.

domain, while HA_2 forms the central helix-rich stem structure.[4] Haemagglutinin is primarily responsible for binding the viral particle to receptors of the host cell. It recognises sialic acid residues on the host-cell glycoproteins and binds tightly to them. Once the virus has been taken into the host cell, haemagglutinin is also involved in the mediation of cell fusion. This releases viral RNA into the cytoplasm of the host, prior to transport into the host cell nucleus for replication.[5] Currently, fifteen distinct subtypes of haemagglutinin have been isolated, most from birds. The four that have been observed in human influenza viruses are denoted H1, H2, H3, and H5.[5]

Neuraminidase makes up approximately 5 to 10% of all viral protein and has a molecular mass of 240 kilodaltons. The native form of this protein is a tetramer, which is anchored to the viral membrane by a long stalk and transmembrane domain, giving it a mushroom-like shape when viewed under an electron microscope. Each monomer consists of six 4-stranded β-sheets arranged in a propeller-like fashion.[6] The active site is located in a deep cavity at the top of the tetrameric spike, which is inaccessible to antibodies.[7] Therefore, although the area is highly conserved, it doesn't aid in recognition of the virus by the host. The function of neuraminidase is to cleave terminal sialic acid residues from both the old host cell and newly formed viral particles. Cleavage from the host cell prevents the newly formed particles from adhering to the old 'used-up' cell, while cleavage from newly formed virions stops them from aggregating. Both of these processes aid in further spread of the virus. The enzyme is also thought to promote elution of newly formed virions from the host cell and their movement through the respiratory tract, although the exact mechanisms by which these processes occur are still unknown.[8] Currently, nine distinct subtypes of neuraminidase are known, of which only N1 and N2 are observed in humans.[5,9]

Influenza Epidemics

Now that we know a little bit more about these viruses, we can look at some of the problems they have caused.

The earliest reported epidemic of influenza was recorded by Hippocrates and Livy in 412 BC.[2] Since then, epidemics of varying severity have been recorded every ten to twenty years. All of these claimed many fatalities due to secondary infections, principally pneumonia.

In this century there have been three major influenza epidemics:

1918-1919 – Spanish flu: Type A(H1N1)
1957-1958 – Asian flu: Type A(H2N2)
1968-1969 – Hong Kong flu: Type A(H3N2)

A double antigenic shift (H1 → H2 and N1 → N2) occurred between the Spanish and Asian flu strains, while a single antigenic shift (H2 → H3) gave rise to the virus responsible for the Hong Kong flu. Of these the Spanish flu was the worst, causing an estimated 20-40 million deaths. That the combined death toll from the two later epidemics was only about 150,000 can largely be attributed to the fact that antibiotics were widely available by this time to help fight secondary infections.

The Spanish flu pandemic struck at the end of World War 1. It actually originated in China but gained it's name due to the absence of wartime censorship in neutral Spain, which, coupled with the fact that King Alfonso XIII was an early sufferer, meant that the first wave of influenza in Spain gained worldwide publicity.[11] An estimated 20-40 million people died worldwide in an 11-month period, with an estimated 20 million fatalities in India alone. The responsible virus was a particularly virulent strain, capable of infecting not only the lungs but also other tissues, including the brain. It seems to have had a preference for the young and fit, and there were many documented cases of people feeling fine in the morning but dying by nightfall.[11]

The first recorded death was in April 1918, but the real problems started in July and August when an antigenic shift is believed to have occurred. The consequent second wave struck almost simultaneously worldwide, with only American Samoa and Iceland setting up successful quarantines. It also struck out of season in many places—the peak in London occurred on the 9 November 1918, only three days before the peak in Auckland. Normally a delay of several months would have been expected between the peak incidence in the Northern and Southern Hemispheres.

The disease landed in Auckland with the troop ship *Niagara* on 12 October 1918. The captain had radioed ahead notifying authorities of 100 cases of suspected Spanish flu onboard, with 25 patients requiring urgent hospital attention. The health minister decided that, since influenza is not a notifiable disease and because 'ordinary' influenza was already rife throughout the country, there was no reason for quarantine. The virus soon spread throughout the country, eventually claiming some 8,500 lives including an estimated 2,100 of the Maori population. The death rate of 42.3 per thousand for Maori was amongst the highest in the world.[11]

The 'bird' flu: Many researchers believe that a major influenza epidemic is long overdue. In 1997, a scare occurred in Hong Kong when the 'bird' flu appeared.

In May 1997, a small boy became sick with influenza-like symptoms and later died. Samples gave negative results for known human strains and eventually the virus was identified as type A(H5N1). This caused much alarm as H5 had previously been observed only in birds.[10] Since the boy came from a farm where infected birds were found, this was initially thought to be an isolated incident. However, a second case was identified in November and by the end of December there were sixteen confirmed cases. On December 28 1997, in a desperate attempt to arrest the spread of the disease, authorities called for the slaughter of all chickens (over 1.5 million) in the markets of Hong Kong, action that many believe saved the world from a great pandemic.

The last case of 'bird' flu was identified on December 28, 1997. In total, there were sixteen confirmed cases, two possible cases and six fatalities.[10] The danger, however, is not over. This particular influenza virus, although virulent, is not readily transmitted between humans. Most of the great epidemics, however, have occurred in two waves, the second caused by a further antigenic shift. This could still occur in the case of the 'bird' flu.

The Viral Life Cycle

An understanding of the life cycle of the influenza virus is crucial if any effective treatments are to be developed.

The life cycle of any virus begins with adhesion to the host cell. In the case of influenza (Figure 1),[5,8] this is mediated by the glycoprotein haemagglutinin and is rapidly followed by internalisation of the viral particle and viral uncoating. The next crucial stage is membrane fusion, which allows the genetic material to enter the cytoplasm of the host cell and then move into the nucleus.[5] It is here that replication of the viral RNA takes place, along with transcription and translation that provide the viral proteins necessary for packaging. Once the new copies of viral RNA are packaged, they are transported to the cell membrane where budding occurs, releasing hundreds of new virions.[8]

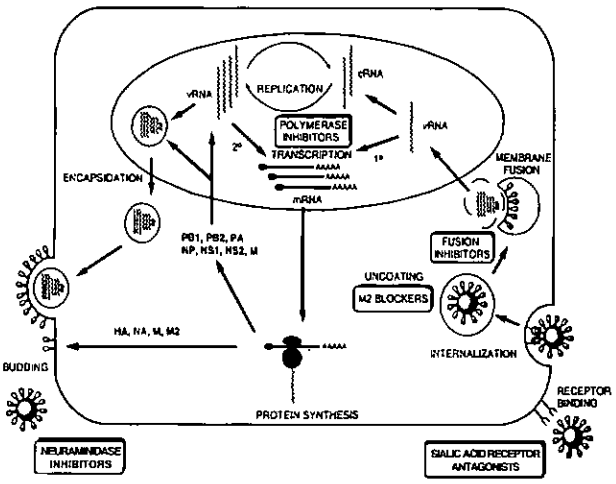


Figure 1: Virus Life Cycle

Vaccinations

The body's first line of defense against infection is the immune system. Vaccinations can be viewed as a means of preparing the body for infection. They are commonly used to control influenza and are currently the best method of prophylaxis (preventative treatment) against the virus.[12] In comparison, known chemical prophylaxes are very expensive and require large, frequent doses.

Vaccination against influenza is recommended for all high-risk patients including:[13]

- people over 65 years of age;
- those with chronic heart, lung or kidney disease;
- diabetics;
- those with immunosuppressive diseases, such as HIV;
- residents of chronic-care facilities.

There are some side effects to vaccination — less than a third of patients experience soreness at the vaccination site, while 5 to 10% show mild flu symptoms.[13]

Currently, 'dead' flu vaccines are used. These contain viruses that have been inactivated by irradiation or chemical means and which, although incapable of causing infection, still evoke an immune response. Flu vaccines are 70 to 90% effective in healthy adults. For the elderly, they reduce hospitalisation by 70% and death by 80%.[13]

Most influenza vaccines contain three viral strains; two of type A and one of type B. But a major conundrum is deciding which particular strains to include. The closeness of the chosen strains to those in circulation determines the level of protection, but the choice must be made months in advance of the flu season's onset. In recent times a computer database has been established, containing amino acid sequence data from viral strains of the last 30 years, to help predict which strains should be incorporated.[14] But despite such technological innovations, major antigenic shifts remain inherently unpredictable.

The company Aviron has recently developed an intranasal flu vaccine, which is intended to reach the market by the 1999 flu season. Their vaccine uses cold-attenuated flu viruses that have been genetically engineered to reproduce in the relatively cool nasal passages but not in the warmer environment of the lungs. Mild strains presented in this manner evoke a wider immune response at the actual infection site,[15] but they do have some problems. For example, the immune system will respond to only one strain at a time when they are presented intranasally. Furthermore, the problem of strain prediction remains, and vaccinations will still be required annually.

Antiviral Agents

Once the influenza virus has entered the body we must look to antiviral agents for any hope of halting the infection. Many such agents have been discovered using high-throughput assays to identify chemical compounds active against influenza viruses. The examples shown in Figure 2 illustrate the structural diversity of such compounds.

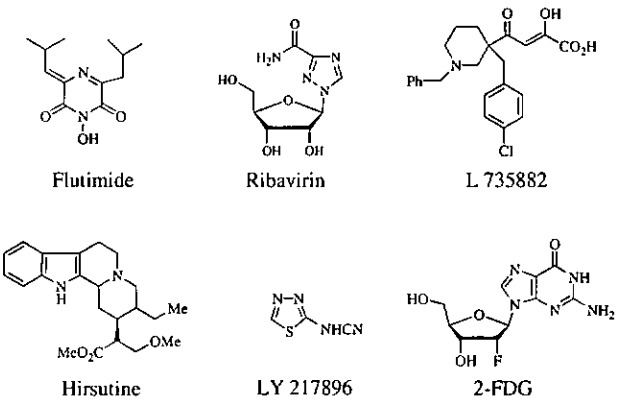


Figure 2: Some Antiviral Agents

Flutimide is an *N*-hydroxyimide derivative, which is isolated from the fungus *Delitschia confertaspora* and is relatively potent against influenza. Structure activity relationship (SAR) studies showed that both the *N*-OH and the level of unsaturation are essential to its activity.[16]

Ribavirin is a broad-spectrum antiviral agent, which inhibits viral replication by interfering with host-cell processes. This can lead to problems of toxicity and immunosupression.[16,17]

L 735882 is a potent and selective inhibitor of influenza endonuclease that shows no evidence of cellular toxicity. The isomer with alkylation *para* to the ring nitrogen is three times more potent and has shown good anti-influenza properties when administered intranasally to mice .[16]

Hirsutine is a monoterpenoid indole alkaloid and a major component of *Uncaria rhynchophylla*, the plant of origin

for the Chinese 'Kampo' medicine used in the treatment of hypertension. This compound is 10 to 20 times more potent than Ribavirin but is only effective against the A(H3N2) strain. The correct stereochemistry is essential for antiviral activity.[18]

LY 217896 — this thiadiazole derivative and its sodium salt both inhibit influenza infections. However, these broad-spectrum antiviral agents interfere with host-cell processes, leading to toxicity problems.[16,17]

2-FDG is the most potent nucleoside inhibitor against the influenza virus. *In vivo*, it is phosphorylated by host cell kinases and then forms a competitive transcription inhibitor. Once again, problems arise with toxicity due to interference with host-cell processes.[16]

Commercial Antiviral Agents

The only two antiviral compounds currently on the market to combat influenza are the aminoadimantane derivatives amantadine and rimantadine (Figure 3).

Rimantadine Amantadine

Figure 3: *Commercial Antiviral Agents*

Amantadine, which goes under the trade name *Symmetrel*, was initially licensed in 1966. It is only effective against influenza A since it acts by blocking the M2 ion channel, which isn't present in influenza B. Blockage of the M2 channel affects the ability of the virus to modulate the pH of the intracellular compartment of the host cell. Since this pH control is essential for the protein conformational change that leads to membrane fusion, the drug prevents any further infection.[19,20]

Resistance of the virus to amantadine arises within three days of initial treatment, making widespread use of this drug infeasible. There are also several serious central-nervous-system side effects associated with this drug,[21] including:

- insomnia;
- nervousness and impaired concentration;
- abdominal pain, nausea and vomiting;
- hallucinations;
- seizure in prone patients.

Rimantadine, under the trade name *Flumadine*, was first marketed in 1993, and has proved more effective against influenza than amantadine. Although side effects associated with rimantadine are less severe, they are still present, and the problem of resistance is similar to that for amantadine.[21]

Haemagglutinin inhibitors

The spread of infection could also be controlled by blocking the activity of either haemagglutinin or neuraminidase. Since haemagglutinin recognises and binds to sialic acid residues, the first compounds investigated for this type of inhibition were simple sialic acid derivatives. Although these do bind to the active site of the enzyme, their overall binding affinity is low, probably due to the fact that they are monovalent, whereas haemagglutinin is known to bind several sialic acid residues at one time.

Polyvalent inhibitors were then investigated.[22] The first of these were constructed from two sialic acid residues linked by chains of various lengths. The example shown in Figure 4 has the highest binding affinity of this series of inhibitors. The distance of approximately 55 Å between the sialic acid residues was shown to be optimal, and is thought to correspond to the separation between receptors on the haemagglutinin-protein complex. Unfortunately, the sialic acid residues in this compound are susceptible to attack and cleavage by neuraminidase, rendering the inhibitor useless.

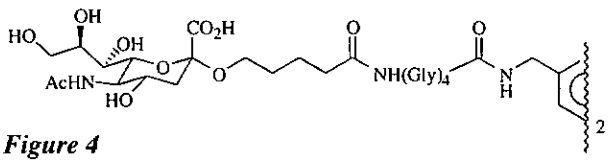


Figure 4

Polymer-based compounds show better binding affinity than dimeric inhibitors.[23-26] The most potent of these is a polymer containing the C-glycoside in Figure 5 on a polyacrylamide backbone.[23] This compound is also resistant to attack by neuraminidase, which increases its potential for use *in vivo*.

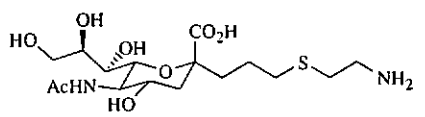


Figure 5

Finally, highly branched 'dendrimeric' compounds, of the type shown in Figure 6, have been synthesised with between four and 32 sialic acid residues per molecule.[27] They have an amino acid backbone, capped with sialic acid moieties and are neuraminidase resistant. These compounds have good binding affinity and inhibition properties, but their potential for possible therapeutic use is untested.

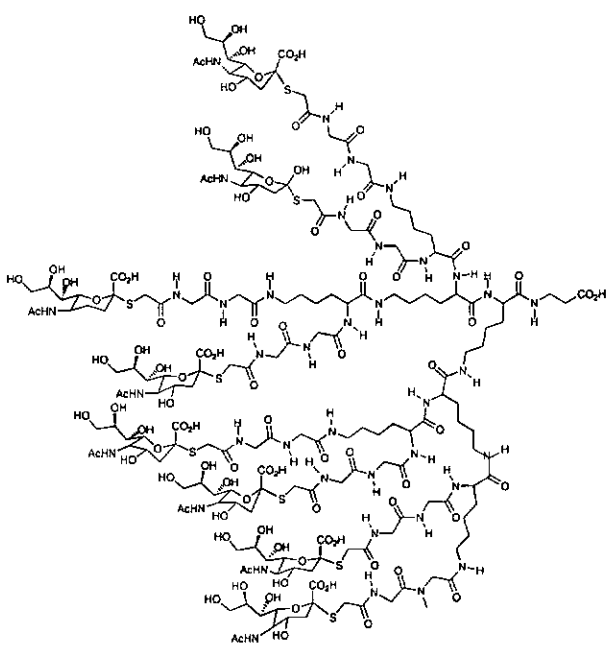


Figure 6

Neuraminidase Inhibitors

Several neuraminidase inhibitors have been identified *via* high-throughput screening programmes. Of these, the earliest investigated were the oxamic acid derivatives — the example shown in Figure 7 is the most potent known so far, but its potential as a therapeutic agent did not warrant further investigation.[16] The dihydroisoquinoline derivative, which was found through investigations of a related chloro compound,[16] was advanced into clinical trials in the late 1960s. It showed some efficacy against influenza B, but never emerged on the market as an anti-influenza drug.

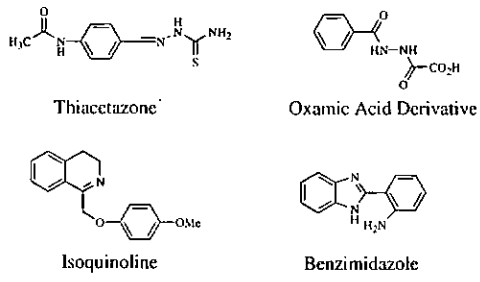


Figure 7: Neuraminidase Inhibitors

Thiacetazone has been shown to inhibit neuraminidase by binding to an allosteric site situated near the Ca^{2+} binding site of the enzyme.[16] Although the role of the calcium ion is unknown, it is essential to activity. The binding of thiacetazone is thought to cause conformational changes in the enzyme, which lead to expulsion of the calcium ion. Thiacetazone is a potent and highly selective inhibitor of the N1 subtype of neuraminidase.[28] It may provide a starting point for further investigations.

The benzimidazole derivative shown in Figure 7 is the most potent of a series of related heterocycles shown to be competitive inhibitors of neuraminidase.[16] It has shown excellent inhibition *in vitro*, but little anti-viral activity *in vivo*. The reasons for this are unclear.

Rational Drug Design

The use of high-throughput assays for potential pharmaceuticals is a bit of a hit or miss affair. An alternative is rational drug design, which involves collection of data about the target enzyme (usually X-ray crystal structures) followed by the design of a specific inhibitor, aided by molecular modelling, to block the enzyme active site.

The challenge of rational drug design in the development of drugs to treat influenza was taken up by a group of Australian scientists.[29] The story began some 40 years ago. In 1961 Dr Graeme Laver (now at the John Curtin School of Medical Research, Australian National University) received world acclaim for his part in the development of a new influenza vaccine, far superior to any in use at that time. He later made use of electron microscopy to identify the shapes of the surface features of the influenza virus. Then in the late 1970s he crystallised neuraminidase.

Laver claims his crystallisation of neuraminidase was (like many great scientific discoveries) an accident. He was working with a solution of the protein when he noticed a sheen on the liquid surface. This was soon shown to be due to the formation of crystals but, since neuraminidase had been previously crystallised in America, Laver initially thought little of the event. It was later to prove extremely important.[30]

In 1978, Laver collaborated with well-known crystallographer, Peter Colman, to take thousands of X-ray diffraction images of these crystals. But the structure proved complicated and elusive and it was four years before the structure was solved and the active site of the enzyme was identified.[30]

Over the following years, crystal structures of several other subtypes of neuraminidase were solved, which showed there to be eleven universally conserved residues in the active site.[6] The quest for this extra information required the crystallisation of many different enzymes—but there are many problems when growing protein crystals, some of which cannot be overcome on Earth. When a crystal is grown in solution, that part of the solution close to the growing crystal edge face will be depleted of protein. The lower concentration will make that part of the solution less dense than the bulk and it may rise, disrupting the growing crystal lattice. Since the less-dense solution will only rise in the presence of gravity, the obvious answer to this problem is to grow crystals in the microgravity of Earth's orbit. The Australian research team therefore turned to NASA, who had performed many protein crystallisations in space. (In fact one of the rationales behind building a space station is to allow such work to continue). NASA scientists successfully grew perfect neuraminidase crystals on the space shuttle, but they were too small for X-ray crystallography. Then the 1986 explosion of the space shuttle *Challenger* ended NASA's part in the crystallisation programme.[31]

Graeme Laver then thought of the Russians and flew to Moscow to request the crystallisation of neuraminidase on the space station *Mir*. Although the officials were somewhat taken aback, they eventually agreed to the plan. The Russians, having never done this type of work before, had to design and build all of the necessary equipment. There was no time for testing, so the equipment and protein were loaded into a shuttle with three cosmonauts and sent to *Mir* in June 1988. The crystals were successfully grown for three months, but problems arose on return to earth. The re-entry vehicle went into the wrong orbit and was left circling the earth aimlessly for some time. Eventually it was retrieved and landed in the Gobi desert with a 'big bang'. On arrival in Australia the crystals were found to be superior to those grown on Earth, and the information was used to verify other findings. However, no new information was obtained, and the whole procedure wasn't really worth the expense .[31]

The 'Plug' Drugs

In 1986, organic chemist Mark Von Itzstein joined the team and took up the synthetic challenge. Sialic acid (Figure 8), the product of the neuraminidase cleavage reaction, is a known weak inhibitor of the enzyme. Consequently, derivatives of this compound formed the first generation of compounds investigated (see *Haemagglutinin inhibitors* above).

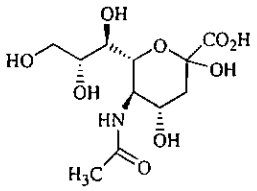


Figure 8: Sialic Acid

Computer modelling showed that the sialic acid derivative deoxydehydrosialic acid (Figure 9) should bind tightly to, and effectively *plug*, the active site of neuraminidase. This compound, believed to be a mimic of the carbocation intermediate, was the first to be synthesised by the group.[32]

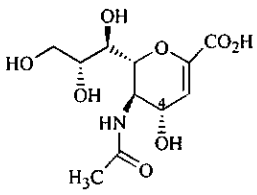


Figure 9: Deoxydehydrosialic Acid

Initial assay studies showed that deoxydehydrosialic acid inhibited influenza in ferrets, a very encouraging result so early in the work. A crystal structure was obtained of deoxydehydrosialic acid sitting in the active site of the neuraminidase enzyme. It clearly showed the hydroxyl group in the 4 position to be sitting directly over a glutamate residue in the active site.[29] Although this residue doesn't appear to play a role in the catalytic cycle of neuraminidase, it is one of the universally conserved residues, and the second generation of compounds was prepared with this in mind.

Further molecular modelling studies showed that replacement of the hydroxyl group at the 4 position by an amino group (Figure 10) should increase the binding affinity due to additional electrostatic interactions with a carboxylate group of the Glu (glutamate) residue.[29] This second-generation compound showed greatly improved activity over the first generation.

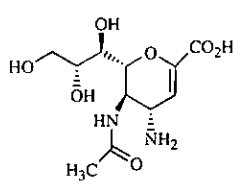


Figure 10

The third generation of compounds resulted from further modelling, which showed that a compound with the bulky guanidino group (Figure 11) should fit snugly into the active site.[29] This compound, named ***GG167***, was synthesised in early 1990 and a crystal structure of it, bound in the active site of the enzyme, was soon produced.

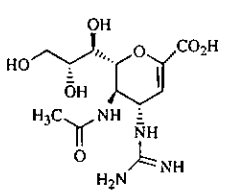


Figure 11: GG167

The strong binding affinity of GG167 is due not only to the additional interaction of the amine with the Glu residue, but also an additional interaction with a second Glu residue of the active site.[33] Assays have shown that this compound was more effective than its second-generation predecessor at concentrations 10 million times lower.[34]

The synthesis of GG167 is complicated by the fact that it contains seven stereocentres that are essential for activity. The synthetic route, shown in Figure 12, begins with sialic acid, which already contains these centres, but the procedure still involves a number of complex protection and deprotection steps to produce the correct overall structure.[17]

GG167 is effective against both influenzas A and B since both of types of virus have the same conserved residues in the active site of the neuraminidase enzyme. It entered clinical trials in 1993 and is being developed and produced, under the name ***Zanamivir***, by Biota Holdings and Glaxo-Wellcome Pharmaceuticals. The poor oral bioavailability of Zanamivir has been overcome by intranasal administration. Clinical trials have shown Zanamivir to reduce the duration influenza symptoms by 20%.[43] There is always the potential problem of resistance but, although resistant influenza strains have been raised in the laboratory, no wild type strains have shown resistance to Zanamivir.[44] It is hoped that the drug will be on the market during this year's flu season under the trade name *Relenza™* (see update on page 19).

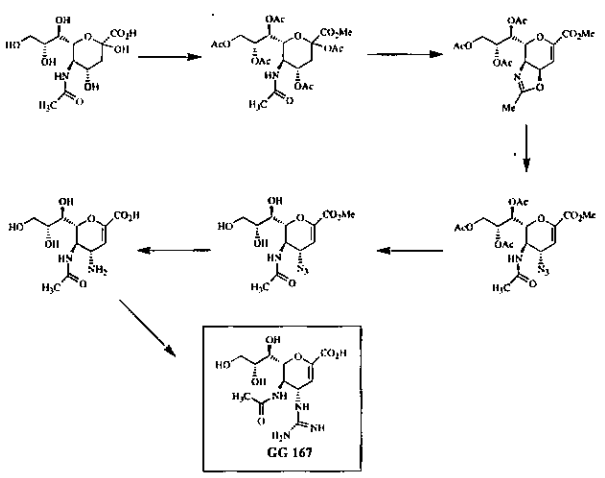


Figure 12: Synthesis of GG167

Many attempts have been made to synthesise inhibitors based on GG167 but requiring simpler synthetic preparations.[16,35-38] These include a series of compounds based on benzoic acid derivatives,[6,39-41] and another series in which the triol side chain is replaced by a branched alkyl ether.[42] One of these ether derivatives, GS4104, has better oral bioavailability and comparable activity to GG167,[19] and has now entered clinical trials.

Flu Diagnostics

Zanamivir (or GG167) is most effective when taken within 24 hours of initial infection.[43] Hence there is a need for rapid diagnostic tests for the disease. Such a test has been developed by Biota holdings. It is called AB FLU OIA and is an optical immunoassay.

AB FLU OIA is based on the selective binding of flu viruses to a surface coated with a compound similar to Zanamivir. A second reagent is then added, causing a visible colour change in a positive test. This assay is able to detect both influenza A and B in about 15 minutes, whereas it currently takes several days to get an unambiguous test result. It is also more sensitive than current techniques and can be used on multiple sample types. It is also hoped that this diagnostic will detect unusual variants, such as the 'bird' flu in Hong Kong, which no current tests are capable of doing.[45]

Conclusion

We have certainly come a long way since the days of the Spanish flu. With the introduction of two new drugs and a diagnostic test onto the market for the 1999 flu season it seems we are definitely making progress in our fight against influenza. It is important to remember, however, that this is a highly variable disease and it is impossible to predict what it may have waiting in the wings.

References

1. Beveridge, W I B. *"Influenza: The Last Great Plague, an unfinished story"*, Heinemann Educational Books, London, 1977.
2. Hope-Simpson, R E. *"The Transmission of Epidemic Influenza"*, Plenum Press, New York, 1992.
3. Information obtained from: http://www.cdc.gov/ncidod/diseases/flu/fluinfo.htm
4. Bizebard, T. *et al.*; *Nature*, 1995, **376**, 92.
5. Laver, G. *Search*, 1997, **28**, 126.
6. Singh, S. *et al. J. Med. Chem.* 1995, **38**, 3217.
7. Varghese, J N. *et al.*; *Nature*, 1983, **303**, 35.
8. White, C L. *et al.*; *J. Mol. Biol.* 1995, **245**, 623.
9. Taylor, N R. *et al.*; *J. Med. Chem.* 1998, **41**, 798.
10. Larson, E. *Time*, 1998 (Feb 23), 34.
11. Rice, G; *"Black November: The 1918 Influenza Epidemic in New Zealand"*, Allen & Unwin, Wellington, 1988.
12. Saul, H. *New Scientist*, 1995 (Feb 18), 26.
13. Information obtained from: http://www.cdc.gov/ncidod/diseases/flu/fluvac.htm
14. Information obtained from: http://www.acl.lanl.gov
15. Information obtained from: http://www.the-scientist.library.upenn.edu
16. Meanwell, N. *et al.*; *Drug Discovery Today*, 1996, **1**, 388.
17. Chandler, M. *et al.*; *J. Chem. Soc. Perkins. Trans. 1.* 1995, 1173.
18. Takayama, H. *et al.*; *Bioorg. Med. Chem. Lett.* 1997, **7**, 3145.
19. Information obtained from: http://www.cdn-news.com
20. Kolocouris, N. *et al.*; *J. Med. Chem.* 1994, **37**, 2896.
21. Information obtained from: http://www.cdc.gov/ncidod/diseases/flu/fluviral.htm
22. Meanwell, N. *et al.*; *Drug Discovery Today*, 1996, **1**, 316.
23. Mammen, M. *et al.*; *J. Med. Chem.* 1995, **38**, 4179.
24. Lees, W J. *et al.*; *J. Med. Chem.* 1994, **37**, 3419.
25. Spevac, W. *et al.*; *J. Am. Chem. Soc.* 1993, **115**, 1146
26. Sparks, M. *et al.*; *J. Med. Chem.* 1993, **36**, 778
27. Roy, R. *et al.*; *J. Chem. Soc. Chem. Comm.* 1993, 1869.
28. Wu, J C. *et al.*; *Biochem.* 1995, **34**, 7154.
29. Von Itzstein, M. *et al.*; *Nature*, 1993, **363**, 418.
30. Information obtained from: http://www.dist.gov.au/events/ausprize/ap96/winners.html
31. Laver, G. *Search (Incorporating Australasian Science)*, 1997, **28**, 156.
32. Taylor, N R. *et al.*; *J. Med. Chem.* 1994, **37**, 616.
33. Von Itzstein, M. *et al.*; *J. Med. Chem.* 1996, **39**, 388.
34. O'Neill, G. *Chem. In Aust.* 1998 (July), 8.
35. Smith, P W. *et al.*; *Bioorg. Med. Chem. Lett.* 1997, **7**, 2239.
36. Starkey, I D. *et al.*; *Tet. Lett.* 1995, **36**, 299.
37. Smith, P W. *et al.*; *J. Med. Chem.* 1998, **41**, 787.
38. Kim, C U. *et al.*; *J. Am. Chem. Soc.* 1997, **119**, 681.
39. Jedrzejas, M J. *et al.*; *Biochem.* 1995, **34**, 3144.
40. Chand, P. *et al.*; *J. Med. Chem.* 1997, **40**, 4030.
41. Chandler, M. *et al.*; *J. Chem. Soc. Perkins Trans. 1.* 1995, 1189.
42. Williams, M A. *et al.*; *Bioorg. Med. Chem. Lett.* 1997, **7**, 1837.
43. Hayden, F. *et al.*; *N. Engl. J. Med.* 1997, **337**, 874.
44. Laver, G. *Search (Incorporating Australasian Science)*, 1997, **28**, 190.
45. Information obtained from: http://www.biota.com.au, http://www.labfocus.com

Relenza™ Update

The Australian flu drug Relenza™ was released on to the New Zealand market in time for the 1999 flu season. On the 29th of June 1999 the pharmaceutical company Glaxo-Wellcome released 4500 units nation-wide.

Early anecdotal evidence is that Relenza™ lives up to its claim that taking it means that you "don't take influenza lying down". The virology department at Christchurch Hospital reported that a staff member, feeling ill, took a diagnostic test and the drug, and suffered only a minor head cold. This is despite the fact that this season's flu strains, one called Sydney A, are proving seriously debilitating. Of course, some may say that well it should, since a week's dosage costs $70 and promises only a reduction in the intensity of symptoms and 36-hr reduction in duration. On the 27th of July 1999 Relenza™ was approved by the FDA, and has since been approved in Australia and by the European Union (which includes countries such as Sweden, France Germany and the UK).

Residue-Free Extraction
A Natural Advantage

Interest in using extracts of natural products for health care is growing, and the ability to extract them without using traditional solvents is proving to be a thriving business opportunity for a Lower Hutt company.

The "nutraceuticals" market is the first target of a new business venture based around Industrial Research's supercritical fluid extraction facility in Wellington.

Local company Supercritical Extraction New Zealand Ltd (SCENZ), has leased the facility for six years and invested heavily to expand its capacity five-fold from a 75-litre operation to a plant capable of producing 375-litre batches.

Sarah Gibbs of SCENZ holds borage seeds and the extract oil - high in γ-linolenic acid.

Supercritical fluid extraction uses a supercritical fluid, in this case carbon dioxide, to extract valuable substances such as essential oils, aromas, and active components from plant and animal material.

The method is gaining popularity as an alternative to extraction using traditional solvents because it is safe, environmentally-friendly, leaves no residues and carbon dioxide is acceptable as a food grade solvent.

SCENZ plans to investigate the market potential of a range of extracts, beginning with the commercial extraction of oils from borage, evening primrose and blackcurrant seeds.

Sarah Gibbs of SCENZ says the oils extracted from these seeds are high in γ-linolenic acid (GLA) for which there is a worldwide market. GLAs are essential fatty acids used in natural heal remedies to help with blood pressure, skin conditions, the menstrual cycle, and cell growth and regeneration.

"There's almost a commodity market for GLA products. We're finding that our evening primrose and borage can command a premium in the market because we use supercritical extraction. The method is pretty new to the natural products market, but they're picking up on it rapidly and we're getting a lot of interest, especially from the USA. We've got the technology they know will be an integral part of the nutraceutical industry in the future."

Although the process is relatively new to the market, Industrial Research has been researching this field since 1986, beginning with a laboratory scale process through to building a pilot plant. Scientists have investigated around 40 different extracts covering spices, herbs, flowers, other plants like hops and manuka, resins, fats, and fish oils.

Supercritical extraction was expensive initially for industry but is getting cheaper and gaining increased acceptance. When using solvents such as ethanol and acetone there are usually residues left in the product. With supercritical extraction the carbon dioxide quickly evaporates leaving no residues.

SCENZ is operating the facility around the clock, seven days a week with a team of four operators. Currently the plant is processing borage and evening primrose seeds which are first crushed and then processed in the extraction vessels.

Whenever possible, SCENZ is sourcing New Zealand grown crops, with borage and evening primrose both being grown locally. Being able to use these local crops was one of the attractions for SCENZ in setting up the venture.

The potential for the supercritical method is enormous as it can also be used to extract compounds for the pharmaceutical and food industries, and there is the possibility of SCENZ doing contract processing work for large overseas companies.

Although the plant has been leased to SCENZ for production purposes, Industrial Research remains in the picture providing technical support and ongoing research work. Currently scientists are helping SCENZ investigate ways to use the waste product from the process, the seed husks.

Sarah Gibbs says having on-site access to this research capability makes the operation quite unique for SCENZ's future clients.

Sourced From: Innovate, September 1999, Industrial Research Ltd.

International News

Experts Say Curb Antibiotics Use

One of the British Government's leading food safety advisory bodies has recommended that the practice of giving antibiotics to farm animals as a preventative measure or to promote their growth should be drastically curtailed, in order to reduce the opportunities for antibiotic-resistant bacteria to emerge. This recommendation follows the release at the end of June of guidelines by the Responsible Use of Medicines in Agriculture Alliance (Ruma), a coalition of farming industry organisations, including the National Farmers' Union and the British Veterinary Association, which also called for an across-the-board reduction in the use of antibiotics in British farming.

In its report, the British Government's Advisory Committee on the Microbiological Safety of Food (ACMSF) claimed that the evidence it reviewed showed 'conclusively that giving antibiotics to animals results in the emergence of some resistant bacteria which infect humans'. Of particular concern, the ACMSF said, were the quinolones and fluoroquinolones, which act by inhibiting DNA gyrase and topoisomerase IV in bacteria, and are invaluable in treating certain salmonella and campylobacter infections. Bacteria resistant to these antibiotics have, however, started to appear and it has been suggested that their use in veterinary medicine, such as the quinolone engrofloxacin used in poultry production, is partly to blame. The report also highlighted the use of antibiotics as growth promoters and recommended that those classes of antibiotics used to treat infection should not also be used to enhance growth. It specifically suggested that spiramycin, tylosin phosphate and virginiamycin be phased out, and added that the remaining growth-promoting antibiotics - avilamycin, bambermycin, bacitracin zinc, monensin sodium and salinomycin - should be more closely controlled.

The European Commission had already announced last year that the use of spiramycin, tylosin phosphate, virginiamycin and bacitracin zinc would be banned from 1 July 1999. This ruling was subsequently challenged in the European Union's Court of First Instance by Pfizer Animal Health, which produces virginiamycin and Alpharma, which produces bacitracin zinc. At the end of June, the court dismissed the challenges, ruling that the threat to public health should take precedence over any economic considerations. The United Kingdom's ACMSF also concluded that the widespread adoption of good farming practices would reduce the amount of antibiotics used by the farming industry. This view was echoed in the guidelines issued by Ruma, which initially deal with only pigs and poultry, but which will eventually be extended to include the dairy, beef and sheep sectors. The Ruma guidelines state that the use of antibiotics should complement good management practice, vaccination programmes and site hygiene. The ACMSF recognised that many of its recommendations would need to be implemented at the Europe-wide level and it seems that the EU commissioner-designate for health and consumer protection, David Byrne, shares the advisory body's concerns. In a statement to the European Parliament recently, Byrne said that if his appointment was confirmed he would implement stringent measures to curb the use of antibiotics as feed additives.

Co-Founder Of J & W Scientific To Receive Award Of Distinction

Walter G Jennings PhD, professor emeritus at UC Davis and co-founder of J & W Scientific, the world's largest manufacturer of high resolution capillary GC columns, was honoured with the Award of Distinction by UC Davis, College of Agricultural and Environmental Sciences on October 15, 1999. The Award of Distinction is the highest recognition presented by the college to individuals whose contributions and achievements enrich the image and reputation of the college and enhance its ability to provide public service. Professor Jennings is recognised worldwide for his outstanding contributions and pioneering achievements in gas chromatography and is considered an expert in hard-surface detergency. Although fully retired from UC Davis as a professor and chemist working with graduate students in the field of gas chromatography, Jennings still works at J & W and continues his close ties to both the industry and the university by conducting seminars, lectures and courses worldwide on the subject of gas chromatography.

NEW ZEALAND INSTITUTE OF CHEMISTRY

NZIC COUNCIL NEWS

PRESIDENT'S MESSAGE

As this is the last issue of *Chemistry in New Zealand* this year, I am taking this opportunity to say that I hope all Members have enjoyed success in 1999 and are looking forward to even better prospects for the coming year and the start of the new millennium. I am writing this brief comment from London, where I am presently on sabbatical leave. While I am overseas, the Vice President, Keith Hunter, is managing any urgent NZIC matters that arise. I will not be back until just after the NZIC Conference to be held at Victoria University of Wellington at the end of November. I hope as many members as possible will attend the Conference and make it a great success. The next national conference will probably not be until December 2001 (because of the Pacifichem 2000 meeting). I remind branch committees that Council now budgets a sum of money each year for Special Project Grants. This is one way that we can confer a greater degree of autonomy on the branches and support new local initiatives. Bids for funds must be prepared and submitted before the first Council meeting of the year, so branch committees should now be considering their plans for the year 2000.

In recent weeks there has been a flurry of activity by the various political parties as the election looms closer and closer. It is very clear from the reports I have seen that education is figuring prominently in the political agenda of all parties as they desperately seek the student vote. I believe that such widespread debate on student fees and equal access to tertiary education is beneficial.

Education is one area where I perceive distinct differences between Britain and New Zealand. The difference is mainly one of emphasis. I am struck by the much greater awareness in the United Kingdom, by pupils and students, parents and the public in general, that a quality education is essential for today's youth. There is great intensity of interest when the GCSE/A-level results are published, as good results provide the platform for entry into one's preferred course and university. I am impressed to see that most primary and secondary schools have uniforms, and every classroom image shown on TV depicts small class sizes and attentive students. I may be old fashioned, but I cannot help wondering whether the discipline of school uniforms doesn't go hand in hand with discipline in the classroom and consequently better academic performance by the students. Despite the public belief in the value of scholastic achievement, the education system in the United Kingdom is nevertheless showing signs of strain. A recent report stated that one sixth of schools are failing to recruit new head teachers, the reasons cited being stress and insufficient financial rewards. I noted with some interest that the head of an average primary school earns about £35,000 (NZ$114,000 at the current exchange rate), the head of a secondary school about £47,000 ($NZ153,000). On the news as I write this today, one head teacher of a new school in London was quoted as earning £70,000 ($NZ227,000). Even these salaries are insufficient to ensure positions of responsibility are filled, and this in a country where teaching is a highly regarded profession. I hope these figures for top salaries in the United Kingdom do not cause an instant mass exodus of our best New Zealand teachers! They do, however, illustrate that New Zealand is falling far behind in the education stakes, and if we are to produce an enhanced "knowledge society", we must be making even more effort to ensure that teaching is recognised as a profession of dignity and standing. We must attract greater numbers of top graduates into teaching positions, and we must reward and support them far more than we do at present.

At the tertiary level in the United Kingdom, the Research Assessment exercise has now been joined by a Teaching Evaluation Assessment. Research funding is directly dependent on research performance, but at the present time no funds flow directly from teaching assessments. However it is expected that this may soon change, and universities are desperately devising ways to improve teaching performance. The 1999 League Tables of the 98 United Kingdom universities have recently been published and these make very interesting reading. Although the individual scores shouldn't be taken too seriously, there is a clear correlation between student:staff ratios and teaching and research assessment results. The top universities, which invariably score well in both teaching and research, enjoy low student:staff ratios (the s:s ratio of the top 5 universities averages 7.2), whereas the under-achieving universities generally score very badly for both teaching and research, and their s:s ratios are high (the s:s ratio of the bottom 5 universities averages 23.0). Translating this to the New Zealand situation, the relentless squeeze on funding which is causing large increases in student:staff ratios in our universities can surely only lead to lower teaching and research qualities, even though we are being continually exhorted to improve both!

I am pleased to see reported in the Royal Society New Zealand *Science Digest*, the Minister of Science's comments on the value of basic research to the nation's future well-being - one of the themes of my talk to the branches earlier in the year. I was taken by an article in the *Daily Mail* on September 17 1999 of the invention of a light bulb using gallium nitride which "provides low power, high intensity, eco-friendly, cheap lighting and

could lead to the world's first everlasting light bulb. ... traffic lights are expected to last 10 years without being changed - instead of six months - with energy needs that are 80% lower than the conventional lighting. Domestic bulbs would never need to be changed in normal use." This is a grand example of how pure chemistry research can spawn new beneficial technological developments, the message many of us have been trying to get over to Government funding providers for some time. I urge all Members to broadcast the successes of our discipline at every opportunity.

George Clark
President, NZIC

BRANCH NEWS

MANAWATU

"Food in the Next Millennium" was the topic for the Branch members to consider at their meeting on Thursday evening 23 September 1999, held at the New Zealand Dairy Research Institute seminar rooms in Palmerston North. Speakers at the meeting were Professor Paula Jameson, Professor of Plant Biology at Massey University, and Mr Jim Kebbel, who runs an organic market garden in Te Horo, Horowhenua and is the Director of the Wellington-based company Common Sense Organics (which retails organic produce). Paula spoke initially on the recombinant DNA technology underpinning the genetic engineering of plants that is leading to the production of genetically modified foods, and then she and Jim discussed the the wider implications of applying genetic engineering techniques to agricultural production. Jim spoke in a discursive but entertaining manner about the risks to society of uncontrolled situations with regard to such genetic engineering. Both speakers were well qualified to present the various viewpoints that have entered into the general debate. Paula Jameson leads a research programme investigating plant hormones and plant development and is also a member of the newly-formed Independent Biotechnology Advisory Council (IBAC). She has spoken previously to audiences on issues relating to genetically modified foods, including the impact of applied genetic engineering techniques on the environment and society. Jim Kebbell is Chairman of BIO-GRO New Zealand, the leading organic certification authority in New Zealand. Earlier this year Jim became convenor of the Organic Federation of New Zealand, a newly-formed group that acts as a watchdog on issues surrounding organic agriculture, and in particular food labelling laws and spray drift. After Paula's and Jim's speeches there was a lively question/answer and discussion session.

In a joint meeting with the Manawatu Branch of the Royal Society of New Zealand at the Science Centre and Manawatu Museum on Tuesday evening 12th October 1999, Professor William Denny, Director of the Auckland Cancer Society Research Centre, School of Medicine, University of Auckland, spoke on "Towards Less Toxic Cancer Treatment: Drug Design Chemistry that Exploits Tumour Biology". He pointed out that while the most successful single design concept for anticancer drugs has been systemic anti-proliferative agents (cytotoxins), these have inherent limitations because among other problems they target dividing cells rather than just cancer cells. One new approach, that builds on the existing knowledge about cytotoxins, is the design of prodrug forms of cytotoxins that are able to be selectively activated in tumour tissue by a variety of mechanisms. A second new approach involves specific inhibition of enzymes in the signalling pathways that control cell division. Many of these enzymes are coded for by oncogenes and are over-produced in tumour cells (there may be about 200 genes, out of the approximately 130,000 human genes that are oncogenetic). Professor Denny discussed the design of enzyme inhibitors with reference to the development of two drugs from the Research Centre, a tumour necrosis factor inducer and an epidermal growth factor receptor inhibitor, both now in clinical trials.

Branch member Benny Theng, Landcare Research New Zealand, attended the Conference of the European Clay Groups Association (EUROCLAY 1999) held at the University of Mining and Metallurgy, in Krakow, Poland, 5-9 September 1999. Benny presented an oral paper "Possible intercalation of fullerene into an organically modified montmorillonite clay", and co-chaired the Symposium on Surface Modification of Clay Minerals and Application of Such Materials. The conference attracted about 400 registrants from various parts of the world, and the programme comprised 11 special symposia and 4 technical sessions. Benny also attended a workshop "Clays in Environment" that was associated with EUROCLAY 1999 but held in Banská Štiavnica, Slovakia, 9-12 September 1999. He presented a poster paper "Bioavailability of phenanthrene intercalated into an alkylammonium-montmorillonite". The workshop included a field trip to a once volcanic region in central Slovakia containing deposits of clay minerals and zeolites.

Harry Percival

1999 NZIC Conference Programme

21-24 November 1999
Victoria University of Wellington

Sunday 21 November

3:00 pm **REGISTRATION COMMENCES** - Ian Gordon Room, Staff Club, Rankine Brown Building

6:00 pm **Baldwin Shelston Waters Mixer & Food,** VUW Staff Club

7:00 pm **PRESENTATION** in the Staff Club
Greg Lynch and Jane Calvert, Baldwin Shelston Waters
The Patent Proze

Monday 22 November

8:00 am **Registration, Maclaurin Foyer**

8:30 am **OPENING CEREMONY** (MCLT 103)
Professor Michael Irving, Vice Chancellor, Victoria University of Wellington
Rob Whitney, Acting President , New Zealand Institute of Chemistry

9:05 am **Ronald Breslow,** Columbia University, (MCLT 103)
The chelate effect in binding, catalysis and chemotherapy

10:30 am **Douglas Russell,** University of Auckland, (MCLT 103)
Looking at chemistry in a different light - application of lasers in fundamental and applied chemistry.

11:10 am **Jim Johnston,** Victoria University of Wellington, (MCLT 103)
Adding value using chemistry - new process and product development

1:00 pm **CONCURRENT SESSION LECTURES:**

ORGANIC SPECIALIST

Emily Parker, Cambridge University, (20 min)
Mechanistic duality of dehydroquinase

Sonya Scott, Massey University (20 min)
Mixed porphyrin and porphyrazine chromophores

John Hoberg, Victoria University of Wellington, (20 min)
Design of bio-active molecules from renewable biomass

Robert McKeown, University of Canterbury, (20 min)
Solubility and structure activity relationships in drugs

Carol Taylor, University of Auckland, (20 min)
Adhesive peptides containing dihydroxyproline

NATURAL PRODUCT SPECIALIST

Peter Waterman Southern Cross University (40 min)
Searching for bioactive compounds: the old and the new

Michele Prinsep, University of Waikato, (20 min)
Slime and scum: natural products from land and sea

George Slim, Industrial Research Limited, (20 min)
Biologically active extracts from the green lipped mussel

Daryl Rowan, Hort Research, (20 min)
Synthesis and biological activity of farnesyl oxidation products

3:45 pm **POSTER SESSION**

6:00 pm Mixer and Food, Maclaurin Foyer

7:00 pm **Professor Sir John Cadogan,** Imperial College, **and Professor Ron Breslow,** Columbia University
Chemistry in the 21st Century

Tuesday 23 November

8:00 am **Registration,** Maclaurin Foyer

8:30 am **Easterfield Medal Presentation**

8:35 am **Bill Henderson,** University of Waikato (MCLT 103)
Bugs, metals and weighing machines

9:20 am **Ian Brown,** Industrial Research Limited (MCLT 103)
Ceramic chemistry - gateway to new technologies

10:35 am **Margaret Brimble,** University of Auckland
Strategies for organic synthesis

11:30 am **CONCURRENT SESSION LECTURES:**

POLYSACCHARIDE SPECIALIST (MCLT 103)

Ruth Falshaw, Industrial Research Limited, (20 min)
Inhibition of Taq DNA polymerase by extracts from New Zealand red seaweeds

Laurie Melton, University of Auckland, (20 min)
Isolating plant cell walls from difficult samples

John Cutfield, University of Otago, (20 min)
How the exoglucanase from Candida albicans *recognises β-(1,3)-glucan substrate: substructure, mutagenesis and activity studies*

NATURAL PRODUCT SPECIALIST (MCLT 101)

Yinrong Lu, Industrial Research Limited, (20 min)
Polyphenols from processing wastes: their characterisation and potential application

Robin Mitchell, Hort Research, (20 min)
Bioactive compounds from pseudomonads

Peter Wigley, BioDiscovery NZ Ltd, (20 min)

1:50 pm **CONCURRENT SESSION LECTURES**

POLYSACCHARIDE SPECIALIST (MCLT 103)

Tony Bacic, University of Melbourne, (20 min)
The structure of the Glycosylphosphatidylinositol-anchor on plant arabinogalactan-proteins

Ian Sims, Industrial Research Limited, (20 min)
*Accumulation of water-soluble carbohydrate in excised leaves of New Zealand flax (*Phormium tenax*)*

Ian Miller, Carina Chemical Laboratories, (20 min)
Regularities in changes of chemical shift on substituted algal galactans

Merilyn Manley-Harris, (20 min)
Kinetics of formation of di-fructose dianhydrides during thermal treatment of inulin

NATURAL PRODUCT SPECIALIST (MCLT 101)

Murray Munro, University of Canterbury, (40 min)
The halichondrins: boom or bust?

Steve Lorimer, Crop and Food Research Ltd, (20 min)
Hodgsonox, a new insecticidal compound?

Kirk Torr, Forest Research Institute, (20 min)
Synthetic analogues of tropolone compounds for enhancing timber biological resistance

3:50 pm **CONCURRENT SESSION LECTURES:**

ORGANIC SPECIALIST (MCLT 103)

Juliet Gerrard, University of Canterbury, (20 min)
Consequences of the Maillard reaction of proteins

Matthew Tilbrook, University of Western Australia, (20 min)
The synthesis of 1233A: an inhibitor of cholesterol biosynthesis

Jim Coxon, University of Canterbury, (20 min)
Ab initio studies of epoxide rearrangements

NATURAL PRODUCT SPECIALIST (MCLT 101)

Noel Porter, Crop and Food Research Ltd, (20 min)
Antibacterial activity of manuka oils

Kevin Mitchell, Industrial Research Limited, (20 min)
Flavonoids of value in the taxonomic revision of the Hebe parviflora *complex*

Peter Northcote Victoria University of Wellington
Anti-inflammatory diterpenes from a New Zealand marine sponge

5:15 pm **Nibbles in the Maclaurin Foyer**

6:00 pm **POSTER PRIZE AWARDS**

6:15 pm **Public Lecture: Professor Sir John Cadogan** (MCLT 103)
From pure science to prosperity

Wednesday 24 November

8:00 am **Registration: Maclaurin Foyer**

8:30 am **Ole Hindsgaul,** University of Alberta, (MCLT 103)
Solid-phase synthesis of carbohybrids and their biological evaluation using frontal affinity chromatography

9:15 am **Dave Lowe,** National Institute of Water and Atmospheric Research, (MCLT 103)
Our atmosphere...a chemical thin film?

10:35 am **Vern Schramm,** Albert Einstein College of Medicine, (MCLT 103)
Enzymatic transition states and the immucillins: transition state inhibitors for N*-ribosyl-transferases*

11:30 am **CONCURRENT SESSION LECTURES:**

FERRIER SYMPOSIUM (MCLT 103)

Arnold Stütz, Technische Universität Graz, (20 min)
Iminosugars and unusual sugar tautomers

David Larsen, University of Otago, (20 min)
Pseudo-sugars, fluorinated carbohydrates and C-glycosides. A Diels-Alder strategy towards their synthesis

Robert Stick, University of Western Australia, (20 min)
Making chemistry merrier with Pherrier – approaches to the synthesis of mechanism-based inhibitors of glycoside hydrolases and synthases

INDUSTRIAL & ANALYTICAL (MCLT 101)

Brett Ammundsen, Pacific Lithium Limited, (20 min)
Lithium-ion batteries: materials solutions for energy storage in the new millenium

Neil Lee, BRANZ, (20 min)
How do you measure the chloride transport properties of concrete?

Gary Massoth, Institute of Geological & Nuclear Sciences (20 min) *Probing the submarine hydrothermal vent environment using an in-site chemical analyser*

Michael Mucalo, University of Waikato, (20 min)
Materials and powders from New Zealand cattle bone

1:50 pm **CONCURRENT SESSION LECTURES:**

FERRIER SYMPOSIUM (MCLT 103)

Stephen Angyal, University of New South Wales, (20 min)
Polyol-cation complexes: a scale for determining the best size for the cation

Peter Tyler, Industrial Research Limited, (20 min)
Convergent synthesis of the immucillins: potent transition state analogue inhibitors of purine nucleoside phosphorylase

Monica Palcic, University of Alberta, (20 min)
Mechanism and inhibition of blood group glycosyltransferases

George Krepinsky, University of Toronto, (20 min)
Side reactions making chemical glycosylations difficult

INDUSTRIAL AND ANALYTICAL (MCLT 101)

Robert Franich, Forest Research, (30 min)
Polymers with a purpose: design, synthesis, testing of polymers to meet performance need

Chris Ferguson, University of Canterbury, (20 min)
Core-shell polymers from vinyl acetate and styrene

Natalia Panova, University of Waikato, (20 min)
The effect of multicomponent equilibria on the precipitation of calcium phosphate for simulated whey permeate solutions

Rod Tilbury, Victoria University of Wellington, (20 min)
Chemiluminescence from bovine serum albumin

3:50 pm **FERRIER SYMPOSIUM** (MCLT 103)

Joachim Thiem, Universität Hamburg, (30 min)
Scope and limitations of chemoenzymatic glycosylation - following and passing nature

Mark von Itzstein, Victoria College of Pharmacy, (30 min)
Sialylmimetics as potential sialidase inhibitors

5:00 pm **Close of Conference**

CONFERENCE DINNER (Te Papa)

6:30 pm **Guided Tour of Te Papa (optional)**

7:30 pm **Pre-dinner drinks**

8:00 pm **Conference Dinner - Rangimarie Suite, Te Papa**
Guest Speaker - Robin Ferrier (will speak between the main course and dessert)

Note - ***MCLT: Maclaurin Lecture Theatre***

Patent Proze

by Jane Calvert and Greg Lynch

PLANT VARIETY RIGHTS

Many readers may be aware that it is possible to protect a new plant variety both by way of a patent and by way of a registered plant variety right (PVR). We previously referred to PVRs in the November/December 1997 issue of Chemistry in New Zealand. We now elaborate further on this form of intellectual property protection.

A PVR may be granted for any new plant variety that meets the requirements of the Plant Variety Rights Act 1987. However, although protection in this manner is possible for fungi, protection is not available for bacteria or algae.

The grant of a PVR may be made for a plant variety if it is:

- new;
- distinct;
- uniform; and
- stable.

New

A variety is considered to be new if propagating material, whole plants or harvested material of it has not been sold or offered for sale with the agreement of the owner:

(i) in New Zealand, for more than one year before the date of application, or

(ii) overseas, for more than 6 years before that date in the case of woody plants, or more than 4 years in the case of non-woody plants.

The owner is expected to have taken every reasonable precaution to ensure that a sale had not taken place earlier than allowed. You may note that the requirements of what is considered to be "new" are more relaxed than the novelty requirement that must be satisfied for patent protection.

Distinct

The variety must be distinct from all commonly known varieties existing at the date of the PVR application. The distinctiveness might arise through a single characteristic or a combination of characteristics. A distinctive characteristic may be physical such as shape or colour, physiological such as disease resistance, or any other characteristic that is distinctive over and above other known varieties.

Uniformity

The characteristics of the variety must remain uniform over a number of plants.

Stability

Despite repeated propagation, the variety must retain its distinctive characteristics.

The Plant Variety Rights Office (located at Lincoln in Canterbury) will usually require inspection of plants and possibly also growing tests in order to ensure the above requirements are satisfied.

The term of a PVR is 20 years in the case of non-woody plants or 23 years in the case of woody plants.

The grant of a PVR provides the owner (typically the breeder or discoverer of the variety) with an exclusive right to produce the variety for sale and to sell propagating material of the variety. Unlike other forms of registrable intellectual property, such as a patent, a PVR application is able to provide provisional protection that is enforceable. In other words, even prior to the grant of a PVR, an owner can enforce the right associated with the variety once a PVR application has been filed.

Further, in the case of vegetatively-propagated fruit and ornamental varieties, the holder of a PVR has the additional exclusive right to propagate the protected variety for the commercial production of fruit, flowers or other products of the variety. Note, however, that other persons are free to:

- grow or use a protected variety for non-commercial purposes,
- use the plants or parts of the protected variety for human consumption or other non-reproductive purposes, or
- use a protected variety for the purpose of plant breeding (although repeated use of a protected variety must be with the authority of the owner of the PVR).

New Zealand plant breeders or developers wishing to obtain plant variety protection in another country must make an application in that country. Because New Zealand is a member of state of the International Union for the Protection of New Varieties of Plants (UPOV), New Zealanders are entitled to apply for plant variety protection in all other UPOV member states.

If you are interested in further information regarding PVRs you may wish to access the excellent website of the Plant Variety Rights Office at http://pvr.govt.nz/index.html. Information is provided on this site about the type of application forms that are required and technical questionaires that must accompany an application. Additionally, there is a searching facility providing information on all granted PVRs and PVR applications.

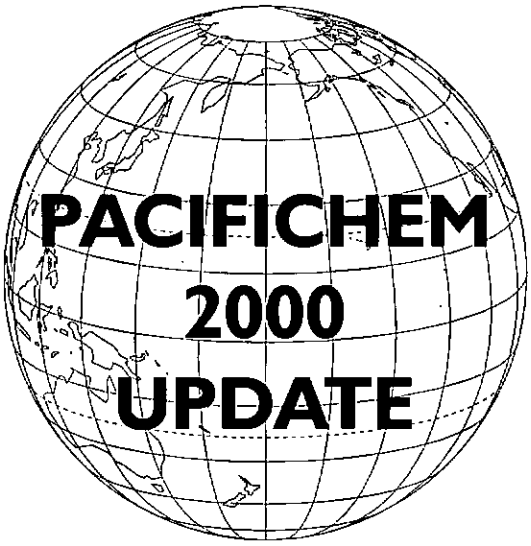
A reminder: If you have any queries regarding patents, or indeed any form of intellectual property, please direct them to:

Patent Proze
Baldwin Shelston Waters
P O Box 852, Wellington
Email: email@bswip.co.nz
Internet: www.bswip.co.nz

Jane Calvert

Jane Calvert and Greg Lynch are both employed in the patent department of Baldwin Shelston Waters, Patent and Trademark Attorneys and Solicitors, where they specialise in chemistry patents. Jane joined the firm after completing a PhD in Chemistry at the University of Canterbury in 1994. Greg also joined the firm in 1994 after three years research at Industrial Research Limited in Wellington. Following completion of a PhD in chemistry at the University of Otago in 1989, he spent a two year period as a post-doctoral researcher at Oxford in the United Kingdom.

Greg Lynch



CALL FOR PAPERS

Papers Sought for Pacific Basin Chemical Congress

Chemists and chemical engineers in countries bordering the Pacific Ocean and in all other countries are invited to submit papers for consideration and to attend the 2000 International Chemical Congress of Pacific Basin Societies. Scheduled for 14-19 December 2000, in Honolulu, Hawaii, USA, it is being cosponsored by the American Chemical Society, Chemical Society of Japan, the Canadian Society for Chemistry, the New Zealand Institute of Chemistry and the Royal Australian Chemical Institute. Many of the Chemical Societies in the countries that border the Pacific Ocean are Official Participating Organisations.

Some 6,000 reports on current research and development will be presented in about 179 symposia in oral and poster general sessions. The Congress will also feature specific scientific events, including plenary lectures, an exposition of chemically-related scientific products and services, and pre- and post-tours of neighbouring islands. General tours will also be offered during the Congress to places on Oahu related to the culture and history of the Hawaiian islands that are not normally part of typical tourist activities.

Papers will be presented in symposia and in general oral and poster sessions in the 10 topical areas in which symposia are grouped (see following pages). A few selected symposia will be for invited papers only. It is a requirement when submitting contributed papers for consideration for symposia or general session presentation in either oral or poster form that an abstract of approximately 150 words be submitted on the special Congress Abstract Form. In November 1999, the abstract form can be accessed on the Pacifichem 2000 Web page at:

http://www.acs.org./meetings/pacific/welcome.htm#2

Abstracts must be in received Washington by 14 April 2000.

All contributed abstracts for papers should be submitted to the Congress Secretariat at the American Chemical Society. Copies of the abstract form and additional information on submitted papers are available from:

Pacifichem Congress Secretariat
American Chemical Society
1155 Sixteenth St, NW, Washington, DC 20036, USA
Email: pacifichem@acs.org

NZIC Secretariat Office
P O Box 39-283 Howick, Auckland
Email: NZICOffice@nzic.org.nz

Professor B Halton
School of Chemical & Physical Sciences
Victoria University, P O Box 600, Wellington
Email: brian.halton@vuw.ac.nz

All details of the Congress including the updated programme listings are available from the web site that can be accessed easily from the Pacifichem listing on the ACS meetings web page at:

http://www:acs.org/meetings

In addition, the full list of symposia for the Congress were published previously together with the details of the Young Scholars Programme in support of chemistry professionals in the developing regions of the Pacific Basin [see: *Chemistry in New Zealand*, **63**, No. 5, 1999 (Sept/Oct), 38-41].

The details for advance Registration, Accomodation, Congress Events and Tours will be published in the July 2000 issue of *Chemistry in New Zealand*. Registration fees have yet to be finalised but approximate figures are $US~350 for full registration (PhD students $US~90); a full list will be published once the rates are set.

IUPAC PRIZE FOR YOUNG CHEMISTS

The IUPAC Prize for Young Chemists has been established to encourage outstanding young research scientists at the beginning of their careers. The prize will be given for the most outstanding PhD thesis in the general area of the chemical sciences, as described in a 1000 word essay.

IUPAC will award up to four prizes annually. Each prize will consist of US$1000 cash and travel expenses to the next IUPAC Congress. In keeping with IUPAC's status as a global organisation, efforts will be made to ensure fair geographic distribution of prizes.

Prizes will be presented biennially at the IUPAC Congress (next congress is to be held in Brisbane, Australia from 1 to 6 July, 2001). Each awardee will be invited to present a talk on his/her research and to participate in a plenary award session.

Applications will be judged by a committee of eminent scientists appointed by the President of IUPAC.

Complete information, including application forms is available on the IUPAC website. The URL is:
http://www.iupac.org/news/prize.html

Artificial Sweeteners

By Maureen Prince, Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch
Email: mjr80@its.canterbury.ac.nz

By far the most commonly used sweetener is sucrose, usually referred to as sugar. Awareness of hazards to health associated with a high-sugar diet has not been sufficient to overcome the human predilection for sweetness. To ameliorate these health problems while allowing people to indulge their liking of sweet things (and at the same time making money) chemical companies have been searching for sugar alternatives – both 'artificial' and natural.

Sugar

β-D-fructofuranosyl-α-D-glucopyranoside, saccharose or sucrose is a disaccharide of glucose and fructose. It is formed in plants by photosynthesis. In sugar cane it is the main storage carbohydrate but in many other plants it is converted to, and stored as, starch, inulin or levin. The transportation of oligosaccharides and polysaccharides in some plant species occurs by conversion to sucrose, translocation and then resynthesis.

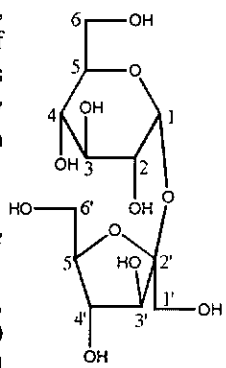


***Figure 1:** Sucrose*

The major source of sugar, accounting for two thirds of the 100 million tonnes of sugar produced annually, is sugar cane. A native of Polynesia, sugar cane was taken to China and then India, where it was first refined into sugar in about 700 BC. Cultivation spread through Persia to Egypt and then to warmer parts of the Mediterranean by 800 AD. The first sugar reached England in 1319 AD as an expensive novelty used mostly in medicines. Its use in Europe was limited and expensive until the seventeenth century, when imports from Carribean plantations became readily available.

During the Napoleonic wars, British naval blockades cut off French sugar supplies from the island of Dominica and French scientists set about the task of seeking an alternative source. They soon discovered that sugar could be extracted from root vegetables such as parsnip and, particularly, the sea beet. Selective cultivation led, within ten years, to the development of sugar beet, which, until last century, was the source of most of the world's sugar.

Crystals of sucrose melt between 185 °C and 187 °C (depending on solvent of crystallisation) and are water-soluble. It is a non-reducing sugar which is readily hydrolysed by acid but is stable to alkali, is heat stable and will keep indefinitely without need for refrigeration. It is relatively cheap to produce and is a good bulking agent. It is not, however, particularly sweet[†].

Disadvantages of Sugar

The average weekly consumption of sugar in the western world is about 750 grams per person, mostly used to satisfy a craving for sweetness. This amount of sugar provides 12,500 kilojoules of energy (16.7 kJ/gram) but has no additional nutritional value.

Following ingestion, sucrose is broken down into fructose and glucose. The latter is the body's main source of energy. It can be converted glycogen, which is stored, in quantities of up to 350 grams, in the muscle and liver tissue. This amount of glycogen will provide approximately 1400 kilocalories, enough energy for one day's activity. Once these storage areas are full, any excess glucose is stored as fat.

Peoples' desire for sweet foods leads to the overeating of sucrose, which, in the developed world, contributes to obesity and consequent ill health. Sucrose is also cariogenic – it is metabolised by plaque bacteria to form acids which attack calcium phosphate in the enamel surface of teeth.

It is clearly in the interests of the people of the western world to reduce their sugar intake. But desire is strong and the will is weak – in affluent nations it is easier (and more acceptable) to find sugar substitutes than to modify dietary habit.

Development of Non-Sugar Sweetners

Sweeteners are classified as bulk or intense, nutritive or non-nutritive.

Bulk sweeteners (including sucrose) are generally carbohydrates or derivatives extracted from plants and other natural sources. They can usually be metabolised to provide energy and are therefore nutritive. Since they are not particularly sweet they are used in large amounts to give the desired sweetness; hence they contribute to the bulk and structure of foods. They also contribute to osmotic, preservation, and bodying (or mouth feel) properties of the food, and they undergo the Malliard reaction, which gives food its brown colour after cooking.

[†] Sweetness is measured by making a solution of the compound in water to known concentration and then asking a panel of people to taste it. The solution is then progressively diluted and tasted until the sweetness can no longer be perceived. The sweetness is always measured relative to sucrose, which is given the value of 1. A point to note is that relative sweetness tends to vary with the concentration of the reference solution. For example, the sodium salt of saccharin is 720 times sweeter than a 2% (by weight) sucrose solution, but only 110 times sweeter than a 10% solution.

Intense sweeteners have a stronger taste and are needed in much smaller amounts. They are usually synthetic compounds and, in most cases, are non-nutritive, providing little if any energy.

Many factors must be considered when developing a new sweetener. The compound should be water soluble, have a long shelf-life and be stable to high temperatures and acidic conditions. Its taste profile should be similar to sugar – a quick sweetness followed by a sharp cut off and no aftertaste. The energy value should be low and the compound and its metabolites should be non-toxic and devoid of undesirable side effects, including the promotion of dental caries. Finally, production should be economical.

Sweetness is determined by panels of people who taste increasingly dilute solutions of a compound in water till they can no longer perceive a sweet taste. The measure of sweetness is given relative to a sucrose solution, which is assigned a value of 1. A point to note is that relative sweetness tends to vary with concentration. For example the sodium salt of saccharin is 720 times sweeter than a two percent (by weight) sucrose solution, but is only 110 times sweeter than a ten percent solution.

Taste panels are also trained to look for certain taste qualities: appearance time (how long till the taste is apparent); extinction time (how long the taste lasts); and flavour profile, including aftertastes which might include, bitter, salty, metallic, cooling or liquorice characteristics. Because some sweet compounds are potentially harmful, they usually undergo mouse toxicity trials and bacterial mutagenicity tests before human taste tests. Behavioural conditioned aversion tests are sometimes used in which the similarity of a compound to sucrose is determined by monitoring the amount of solution consumed by Mongolian gerbils trained to avoid sweet, salty, sour and bitter taste qualities. The reliability of this assay method was determined using known sweet compounds as controls.

Many thousands of molecules elicit a sweet taste. The final choice of sweetener is influenced most strongly by the consumer. Public concern over artificial or synthetic food additives has seen an increasing attention devoted to sweeteners from 'natural origins'. But most of the alternatives currently in use are synthetic or 'artificial'.

Intense Synthetic Sweeteners

Sapa. The first recorded artificial sweetener, discovered by the Romans and called sapa, was prepared by boiling grape juice, wine lees or soured wine in a lead pan to produce a sweet syrup. Wine contains acids such as tartaric and citric acid. If it also picks up spores of the common *Acetobacter* the alcohol is converted to acetic acid which is sour. When boiled, the acetic acid reacts with lead to produce lead acetate, a sweet but toxic compound that is also known as sugar of lead.

Sapa was used to sweeten foods and also to 'improve' wines – it killed the bacteria that caused the wines to sour.* It was also popular amongst prostitutes because it gave them a pale complexion and had a contraceptive effect. The Romans were rightly suspicious of sapa. It was reported to make people tired and listless, anaemic, constipated and infertile, but it did taste nice.‡

Saccharin. American scientist Ira Remsen and Russian-born Constantin Falhberg discovered saccharin (3-oxo-2,3-dihydro-1,2-benzisothiazole-1,1-dioxide) at the John Hopkins University in 1879, at a time when it was common practise to include taste in the characterisation of chemical compounds. Saccharin is about 300 times sweeter than sugar and is most commonly synthesised as a sodium or calcium salt. It has good stability in conditions prevalent in food preparation and has been used as a sweetener for about 80 years. For a time it was the only non-sugar sweetener available.

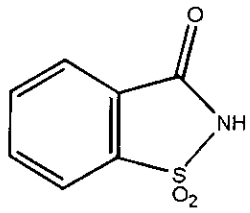


***Figure 2:** Saccharin*

Saccharin cannot be metabolised and is therefore non-nutritive. Its main use has been in weight-control and diabetic products, vitamin preparations and toothpaste, although many people find it to have a metallic or bitter aftertaste. In terms of dental safety, saccharin is a very good sweetener. It exhibits a degree of inhibition of the microorganisms associated with dental caries and may also curb dental plaque formation.

Since the discovery of bladder tumours in rats fed with high levels of saccharin, there has been a lot of debate over its safety. However, numerous studies and expert committees have concluded that it is safe for humans even in very high doses.

Saccharin is currently used in more than ninety countries, often in a blend with other sweeteners to give a synergic sweetening effect. For example, a ten-to-one mixture of saccharin with cyclamate gives a product that is sweeter than either in their pure forms.

Cyclamate. Cyclamate, or cyclohexal sulfamate, was discovered in 1937 by Michael Sveda at E.I. DuPont de Nemours. On placing his cigarette on the laboratory bench (a practice that would be highly frowned upon today) he accidentally contaminated it with the compound he was working on. When he next took a drag he experienced a sweet taste.

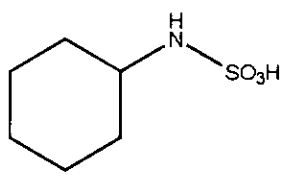


***Figure 3:** Cyclamate*

Cyclamate is available in its acid form or as a sodium or calcium salt. It is thirty times sweeter than sugar, but only a tenth as sweet as other artificial sweeteners and so quite large quantities are required. Its taste profile has a slow onset and is quite persistent. It is stable to temperature and sufficiently soluble for use in drinks and as a tabletop sweetener.

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* Until last century vintners still used the trick of adding a lead pellet to wine to improve the flavour and prevent souring.

‡ Other sweet inorganic salts include $BeCl_2$ and $BeSO_4$, which are also toxic.

In the mid 1960s cyclamate dominated the market for artificial sweeteners. In 1970 it was banned in some countries after a high incidence of bladder cancer was found in rats fed a blend of cyclamate and saccharin – even though those doses corresponded to the consumption by humans of 800 cans of soft drink a day.

Cyclamate is metabolised only by a very small population of people, its major metabolite being cyclohexylamine. Tests on the compound and its metabolites have failed to show potential for carcinogenicity. It has synergistic effects with other sweeteners and is widely used in low-calorie foods and drinks.

Acesulfam K. Acesulfam K is the common name for 6-methyl-1,2,3-oxathiazine-4(3H)-one-2,2-dioxide, which is sold under the trade name *Sunnett*. It was discovered, once again by chance, by Karl Claus of Hoechst who licked his fingers to pick up a piece of weighing paper. It is chemically similar to saccharin but has an improved aftertaste and is approximately 200 times sweeter than sugar.

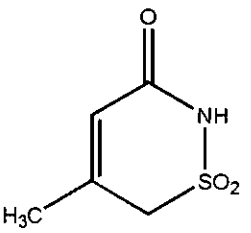


Figure 4: Acesulfam K

Acesulfam K is stable in water, acidic conditions and to high temperatures. It is not metabolised by the body and has shown no adverse side affects. Unfortunately its taste profile includes a bitter note. Acesulfam K is used in some foods, soft drinks, toothpastes, mouthwashes and pharmaceuticals.

Sucralose. (1,6-dichloro-dideoxy-β-fructofuranosyl-4-chloro-α-D-galactopyranoside) is a chlorinated derivative of sucrose. The sweetness of this and other sucrose chloride derivatives was discovered by Shashikant Phadnis who, when asked by a sugar company for samples to 'test', thought that they said 'taste' and tried them himself.

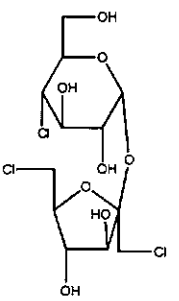


Figure 5: Sucralose

Derivatives have been made with chlorine atoms replacing various hydroxyl groups in the sucrose molecule. The sweetest, with chlorine atoms at the 4, 1′, 4′ and 6′ positions, is 2000 times sweeter than sucrose. The product with chlorine atoms at the 2, 6, 1′, and 6′ positions is extremely bitter. The derivative with chlorine atoms on the positions 4, 1′ and 6′ is 650 times sweeter than sucrose. Although less sweet than the tetrachloro derivative, this trichlorogalactosucrose molecule is easier to make, and is used as a sweetening agent under the trade name *Sucralose*.[1]

Sucralose is not metabolised and is therefore non-nutritive. It is crystalline, water soluble and stable to high temperatures and acidic conditions, but is very slowly hydrolysed to monosaccharide units. Its taste profile is very similar to sucrose and it has no bitter aftertaste. Having passed all necessary safety tests, *Sucralose* is currently approved for use in Canada, Australia, Mexico, Russia and Romania.

Aspartame. The sweetness of aspartame was discovered in 1965 by James Schlatter who was working on anti-ulcer drugs for the company G D Searle and Company of Stoke, Illinois. About 200 times sweeter than sugar, it is known for its good taste profile and flavour enhancing qualities. It is sold in about fifty countries around the world under the trade names *Canderel* and *Equal* but is best known by the brand name *Nutrasweet* which is actually an aspartame–saccharin blend.

Aspartame is a dipeptide of the amino acids, L-phenylalanine-1-methyl ester and L-aspartic acid. It is metabolised like any other protein and is therefore nutritive, but because so little is actually required its energy contribution is negligible. The presence of phenylalanine makes aspartame a potential health hazard for people who suffer from phenylketonuria, an absence of the enzyme that metabolises phenylalanine. Other drawbacks include its low solubility and instability in aqueous, acid and high-temperature conditions, which make it unsuitable as a sweetener in cooked foods. Aspartame decomposes at a rate of ten percent a month at room temperature, which limits its use to foods with a high turnover, such as soft drinks and fruit yoghurts.

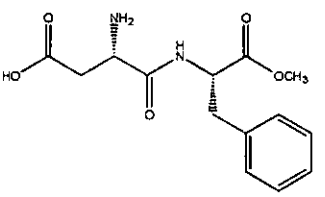
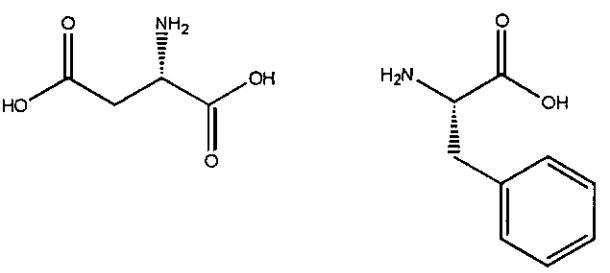


Figure 6: Aspartame

Aspartame is a poor nitrogen source for dental microorganisms and inhibits their growth and metabolism. This positive dental attribute is best when aspartame is used in combination with saccharin.



ASPARTIC ACID PHENYLALANINE

Figure 7: Aspartic acid, phenylalanine

Aspartame was first approved for use in 1974, then banned in 1975 before being reinstated again in 1981. Today it accounts for more than seventy-five percent of complaints about adverse food-additive effects to the United States Food and Drug Agency. Rather than aspartame *per se*, it is probably the metabolites aspartate, phenylalanine, methanol and diketopiperazine, that are responsible for these problems: headaches, dizziness, seizures, nausea, numbness, muscle spasms, joint pains, rashes, depression, fatigue, irritability, tachycardia, insomnia, vision problems, hearing loss, heart palpitations, breathing difficulties,

[1] Of the derivatives containing other halogens, only those with bromine have an enhanced sweetness. Fluorine is believed to be too electronegative and iodine too large to give a sweet molecule.

anxiety attacks, slurred speech, loss of taste, tinnitus, vertigo, memory loss and weight gain.*

Alitame. Aspartame's main rival is the amino acid-based sweetener alitame (L-α-aspartyl-N-(2,2,4,4,-tetramethyl-3-thietanyl)-D-alaninamide), developed by Pfizer Central Research. During its development, careful consideration was given to the effect of substituents on stability, sweetness and flavour attributes. The final compound is by no means the sweetest of its type but was chosen due to its synthetic accessibility. It is 2000 times sweeter than sugar and ten times sweeter than aspartame.

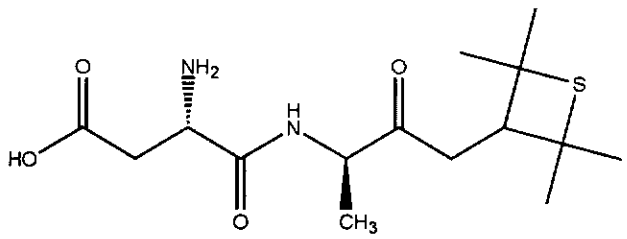


Figure 8: Alitame

Alitame has been shown to be safe up to 200 times the estimated chronic intake of 0.34 mg/kg of body weight. It is a crystalline, odourless, non-hydroscopic compound of good solubility. It has a good thermal stability and shelf-life, although the flavour diminishes with prolonged storage in acidic media due to hydrolysis. The aspartic acid component is metabolised, while the alanine amide metabolite generally passes through the body unchanged.

Aspartyl – diaminoalkanes. This new class of compounds involves modification of L-aspartyl-D-alanine amides were the terminal amide group is converted to an amine using phenyl iodosyl bis(trifluoroacetate).

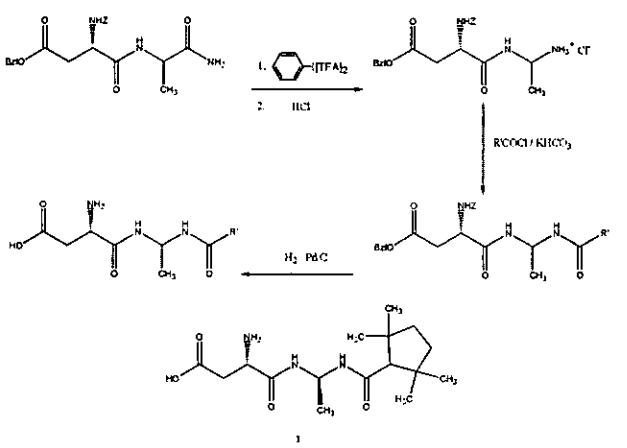


Figure 9: Scheme and tetramethylcyclopentyl derivative

Of a series of compounds synthesised, the tetramethylcyclopentyl derivative (**1**) is 600 to 800 times sweeter than sugar but with a similar taste. These new sweeteners are very stable to hydrolysis.

Intense Natural Sweeteners

Although sweet compounds may feasibly be present in microorganisms, marine organisms and lower order plants, all naturally occurring sweeteners discovered to date have been derived from higher order plant species. 75 plant constituents are known to be sweet. They represent 20 different structural types of compounds including sesquiterpenes, triterpene glycosides, dihydroflavonols and proanthocyanidins.

Stevia. There are more than 180 species of the Stevia plant but *S. rebaudiana* is the sweetest. Natives of Paraguay and Brazil have used the leaves of Stevia as a sweetening essence for centuries. Traditional uses include flavouring agents, herbal teas and medicines. Eight sweet entkaurene glycosides have been identified from the leaves of Stevia, the principal one being Stevioside.

Stevioside has been found in quantities of up to 10% (by weight) and is extracted as a white crystalline hygroscopic powder that is 300 times sweeter than sucrose. It has a slow latent sweetness, but also a strong bitterness and an unpleasant aftertaste. The bitterness is reduced in the presence of sugars such as sucrose, glucose or fructose. Stevioside is stable up to 95 °C and so is suitable for use in cooked foods, but it is not very soluble in water. It is also non-calorific, non-fermentable and doesn't undergo any Malliard-type reactions.

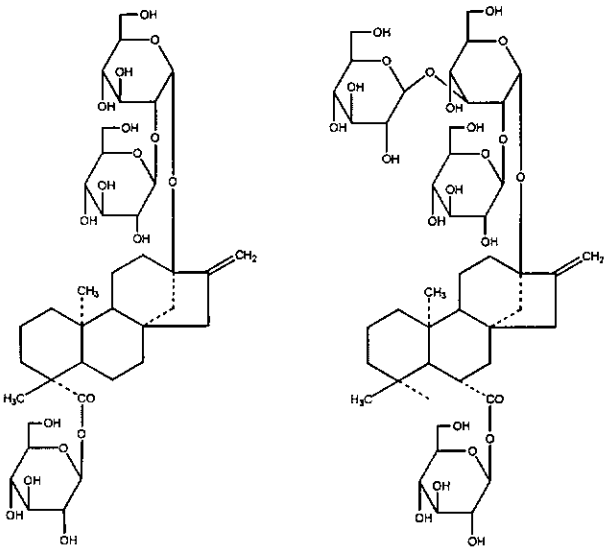


Figure 10: Stevioside (left), Rebaudinoside A

Rebaudinoside A is the next largest constituent of the stevia leaf and has a sweetness 400 times that of sucrose. Unlike Stevioside, it is very soluble in water, but it too has a bitter after taste (though not as bad as Stevioside). Due to its more desirable properties, Rebaudinoside A has been chosen for development on a commercial scale in Japan. To minimise the bitterness of the compound new extraction methods and different strains of the plant have also been developed.

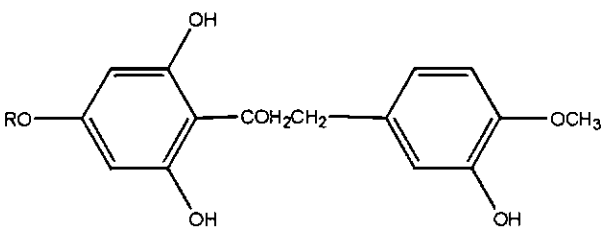
The best tasting Stevia plant is grown in Paraguay where the climate is most suitable. Other varieties have a more intense bitter component and what is described as a grassy taste. Bitter tasting compounds are found to have the greatest concentration in the veins of the leaf while the sweet material is concentrated between the veins. Stevia has been used as a sweetening agent in Japan, China, Korea,

* In the United States, thousands of products contain aspertame: consumption of this compound is probably very much greater than it is in New Zealand.

Taiwan, Israel, Uruguay, Brazil and Paraguay for many years. Both Stevioside and Rebaudinoside A are commonly used in Japan for soft drinks, soy sauce, pickled vegetables and confectionery.

Stevia has been used as an antimicrobial agent, a digestive tonic and as a treatment for diabetes, cardiovascular complaints and skin problems. There have been no reports of ill health due to stevia in its 11,500 years of use. All safety tests of Rebaudinoside A and its metabolites have shown it to be safe for human consumption. Stevioside is not metabolised as its structure is very resistant to acidic and enzymatic cleavage. All toxicity tests have proven it quite safe. However, a metabolite of Stevioside, steviol, which is thought to be toxic, has been formed in the caecum of rats and both Stevioside and Rebaudinoside A can be metabolised to aglycone, a mutagenic, when fed to rats. Never the less, at present it has not been shown that this metabolism occurs in humans.

Neohesperidin Dihydrochalcone (NHDC). This sweetener is synthesised by hydrogenation of Neohesperidin, which is a naturally occurring flavonoid found in citrus peel. NHDC is several hundreds of times sweeter than sugar with no bitter aftertaste. Its sweetness is relatively long lasting so it is normally combined with other sweeteners. It is also relatively stable over a wide range of temperatures and acidity conditions. In its pure form NHDC produces bitter, liquorice and cooling sensations. NHDC is mostly metabolised, although a small percentage can be excreted unchanged.

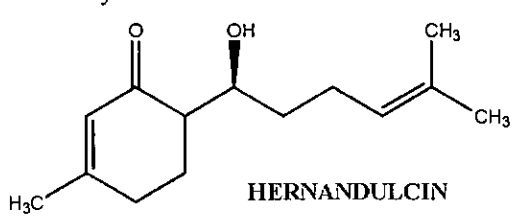


NEOHESPERIDIN DIHYDROCHACONE (NHDC)

Figure 11: NHDC

This compound has currently been approved for use in Belgium and Argentina, mainly in soft drinks and chewing gum.

Hernandulcin. Hernandulcin is a sweet sesqiterpene found in the leaves and flowers of the plant *Lippa dulcis.* It has been prepared chemically as a racemate, but its isomer epihernandulcin is tasteless. Unfortunately in spite of its intense sweetness, Hernandulcin has a bitter aftertaste that makes it unsuitable as a sugar substitute. It is hoped that chemical alterations will enable removal of the bitter functionality.



HERNANDULCIN

Figure 12: Hernandulcin

Glycyrrhiain. This compound is a triterpenoidsaponin found in the roots of the licorice plant. It is 50 - 100 times sweeter than sucrose and not surprisingly, has a definite liquorice taste. Glycyrrhizin can be hydrolysed in the intestine to release a sugar moiety, glucuronic acid, that can then bind plasma proteins and enter with them into the enterohepatic system and be completely metabolised.

Glycyrrhizin has many pharmacological properties including antiviral, antiulcer, antiinflammatory and antispasmodic activity. It has corticoid action by influencing steroid metabolism and it maintains blood pressure and volume. It is also involved in regulation of the glucose/glycogen balance. Glycyrrhizin is thought to be non-carcinogenic and its medicinal properties give it a variety of oral applications, other than just a sweetener. The ammoniated salt of glycyrrhizin acid is available as a flavouring agent and as a surfactant, although the latter applications are limited due to its taste.

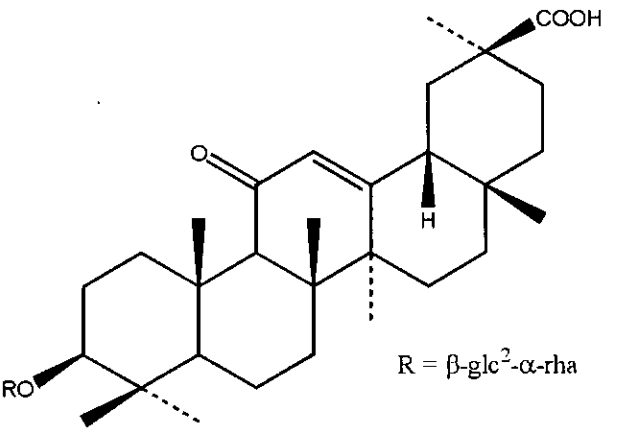


Figure 13: Glycyrrhian

Thaumatin. Thaumatin is a naturally occurring, liquorice tasting protein that comes from the fruit of a West African plant ketemfe, (*Thaumatococcus daniellii*) and has the trade name *Talin.* It is a large polypeptide consisting of two separate but related proteins with a total molecular mass of 20 kD. Although it is 3000 times sweeter than sugar – much sweeter than most artificial sweeteners, the onset of the sweet taste is slow. Unfortunately, the polymer structure of Thaumatin limits its use as a sweetener. It has many recognised sweet-receptor binding sites, so it clings to the tongue and its taste has a lingering effect. This characteristic is good for products such as chewing gum but prevents its use in many foods. Thaumatin is predominantly used as an additive to pet foods, but is permitted in some countries as a flavour enhancer for use in toothpastes and mouthwashes. Widespread use of Thaumatin has been undermined by its high price, but this may be overcome soon as the gene responsible for its production has been introduced to microorganisms in the hope that it can be produced more efficiently. Because Thaumatin is a naturally occurring polypeptide it doesn't have any toxicological problems and has been found to be safe for consumption in quantities 80,000 times greater than the expected levels of intake.

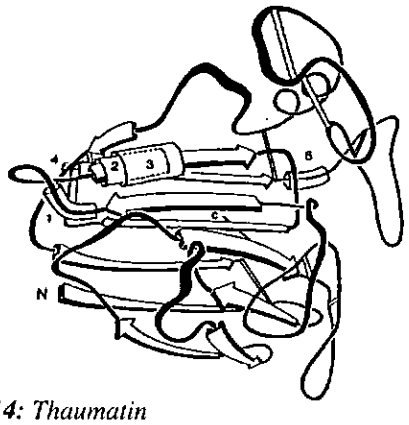


Figure 14: Thaumatin

Monellin. Monellin is a sweet protein from the serendipity berry (*Dioscoreophyllum cumminsii*). It is 3000 times as sweet as sucrose and has a molecular weight of 11.5 kD. It is comprised of two amino acid chains, neither of which by itself tastes sweet. The sweetness of Monellin is destroyed when the protein is denatured in hot or acidic environments.

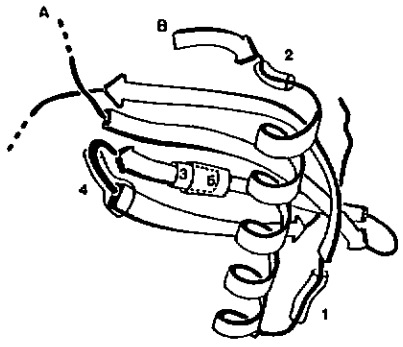


Figure 15: Monellin

Although Thaumatin and Monellin are both intensely sweet proteins, they possess very little sequence similarities. They do however both contain five pairs of homologous triplets. It is thought that a combination of two or three of these sites may be responsible for the observation that antibodies raised against Thaumatin cross-react and compete for Monellin as well as other sweet tasting compounds.

Some advantages of these two proteins over other artificial sweeteners are:

- Although nutritive they are low in calories due to their high potency.
- They are safe and natural.
- The genes that code for these proteins could be cloned in order to mass-produce the proteins.
- The amino acid sequence in the proteins could readily be modified to enable variations that give more desirable taste or physical properties.
- The sweet genes could feasibly be cloned into plants, fruits or microorganisms.
- Due to their high potency, proteins could be used to isolate the sweet receptor(s).

Miraculin. Miraculin is a glycoprotein isolated from the miracle fruit (*Richadella dulcifica*) with a molecular weight of 42 kD. The protein itself is tasteless but when added to a sour tasting compound it can result in a taste 400,000 times sweeter than sucrose that may last for over 24 hours. It is heat labile but inactivated in acidic conditions.

Synergic Sweetening

The desirable properties of a sweetener may be achieved by blending together a selection of sweeteners with a variety of structures and metabolic pathways. One advantage of this approach is that the amount of each sweetener used may be kept well below the level at which doubts exist about its safety. It has been shown that a synergistic advantage may exist in binary or ternary mixtures. That is, the combination of two or three compounds can result in a mixture that is sweeter than any of the individual components. The sweetest mixtures occur when a bulk sweetener is combined with an intense sweetener. In these cases the advantages found in both types of sweetener complement each other, while any negative features are markedly reduced.

References

1. Chemical societies review, Haworth memorial lecture: The sweeter side of chemistry by Leslie Hough 357-374.
2. *Chemistry and Industry*, 4 April 1988, 228-234: Utilisation of sucrose as an industrial bulk chemical - state of the art and future implications. Hubert Schiweck, Knut Rapp and Manfred Vogel.
3. Life with Stevia: How sweet it is! Nutritional and Medicinal uses. Daniel Mowrey PhD http://www.healthfree.com/herbgarden/stevlife.htm
4. The bitter truth about artificial sweeteners. Mark D Gold http://www.tiac.net/mgold/users/health.html
5. Symposium: Sweeteners and sweetness theory. *Journal of Chemical Education*, **72**, 8, August 1995, 671-683.
6. Sweeteners a question of taste. Gordon G Birch, *Chemistry and Industry*, 3 February 1997, 90-94.
7. Prospects for sugar substitutes. T H Grenby, *Chemistry in Britain*, April 1991, 342-345.
8. The sweet taste of success. Lisa Oxlade, *Chemistry in Britain*, March 1991, 198-199.
9. Sweet glycosides from the stevia plant. B Crammer and R Ikan, *Chemistry in Britain*, October 1986, 915-918.
10. Designing sweetness to order. John Emsley, *New Scientist*, 31 October 1985, 22.
11. Sweeteners: Bitter sweet inversion. David Bremner, *Chemistry in Britain*, January 1986, 11.
12. A new class of amino acid based sweeteners. William D Fuller, Murray Goodman and Micheal S Verlander. *J. Am. Chem. Soc.* 1985, **107**, 5821-5822.
13. The shape of sweeteners to come. Leslie Hough and John Emsley, *New Scientist*, 19 June 1986, 48-54.
14. The consumers good chemical guide. John Emsley, *Pub.* W H Freeman, Specktrum: Oxford, N.Y., Heidelberg . W H Freeman and Co. Ltd. 1994.
15. Food Chemistry, H-D. Belitz, W Grosch, Springer - Verlag Berlin 1986.
16. Sweeteners: Discovery, Molecular design and Chemoreception, *Ed.* D Eric Walters, Frank T Orthoefer, Grant E. DuBois, American Chemical Society 1991.
17. Food Chemistry 3rd edition. *Ed.* Owen R Fennema, *Pub.* Marcel Dekker Inc. 1996.

Report on Attendance of the 40th General Assembly and Council Meeting of the International Union of Pure & Applied Chemistry (IUPAC)

Free University, Berlin, 6-14 August 1999

Patrick Holland, HortResearch, Private Bag 3123 Hamilton

1. IUPAC General Assembly

I attended the general assembly as an elected member of the Committee for the Division of Chemistry & the Environment. An edited summary of the minutes of our activities over four days follows. I also attended some of the meetings of the Commission on Agrochemicals & the Environment and contributed to project work.

1.1 Restructuring of IUPAC

The program of change approved by the Bureau is designed to improve the quality, relevance, international impact and effectiveness of the Union's scientific work by:

- revitalising long-range planning within the Divisions
- ensuring the selection of only high quality projects to bear the IUPAC label
- encouraging participation by the world-wide chemistry community
- optimising the use of IUPAC's limited financial resources; and
- simplifying management and accountability.

It was confirmed that all Commissions, Working Parties and Interdivisional Committees will be terminated at 31 December 2001. It will largely be up to the Divisional Committees to decide on appropriate management structures for continuation of high priority work. Some Commissions could be reinstated but this was seen as the exception and would require Bureau approval. A project driven structure is seen as more generally appropriate using 'task groups' of 3 – 5 year duration to plan and execute major programs of work. Projects will be initiated from within or outside IUPAC. The link of Titular membership to funding will be broken with funding for participation in each project being decided on need. Funding priorities for larger interdivisional or external collaboration projects will be decided by a Project Committee set up by Bureau.

There was considerable discussion of the implications of these changes. The Divisional Committees will have enhanced responsibilities and workload. The dissolution of Commissions will require development of other avenues to maintain the 'people power' inherent in the current system for generation of ideas and ensuring high quality outputs. While some money will be freed up by release of Titular funds from less active Commissions, projects will remain largely dependant on voluntary inputs. The ability for task groups to meet and progress several projects simultaneously was seen as important to efficient use of the limited funds. Intensive planning must take place to ensure a smooth changeover at 2002.

1.2 Membership of Division 6, Chemistry and the Environment (DCE)

The following executive was elected for the period 2000 – 2001 with a committee of nine, including the chairpersons of the five commissions:

Dr W Klein (Germany)	- Division President
Dr K Racke (USA)	- Vice-President
Dr J Miyamoto (Japan)	- Past President
Dr P Holland (New Zealand)	- Secretary

The division has five commissions (elected chairperson for 2000-2001):

Fundamental Environmental Physical Chemistry (Professor D Turner, Sweden)
Atmospheric Chemistry (Professor T Tavares, Brazil)
Soil and Water Chemistry (Dr Y Shevah, Israel)
Agrochemicals & the Environment (Dr K Racke, USA)
Food Chemistry (Dr J Gilbert, UK)

1.3 DCE - Terms of Reference, Future Direction and Current Work

Through its internationally recognised membership, the DCE will provide unbiased and timely authoritative views on the behavior of chemical compounds in the environment. The DCE intends to undertake both fundamental and applied chemical studies aimed at solving environmental problems. In this way DCE contributes to global sustainable development.

The Division President Dr Miyamoto summarised the desired direction of DCE activity:

- Effective and efficient operations during the transitional restructuring period of IUPAC
- Integration and expansion of current activity in terms of multidisciplinary aspects, e.g. chemical aspects of increased quality food production and environmental risk assessment
- Closer coordination and collaboration with outside organisations for the mission oriented activities of IUPAC.

Most of the meetings at the General Assembly were devoted to reviewing current projects in the Commissions,

determining priorities for new projects and associated budgets for 2000-2001. A number of workshop type projects in developing countries were proposed as very appropriate ways for DCE to assist IUPAC achieve its goal of contributing to global development and solution of environmental problems. Records for all approved projects are now maintained on the IUPAC Web site. Progress reports and, in many cases, final reports can be found at this site: http://www.iupac.org/project

Two half-day mini-symposia at the Free University of Berlin were organised by DCE on the themes:

- Contributions of Chemistry to Ameliorating Environmental Contamination; and
- Contributions of Chemistry to Sustainable Food Production

2. IUPAC Council Meeting

I attended the council meeting as the representative of the Royal Society of New Zealand and carried 2 votes out of the total of 133 from the 43 National Adhering Organisations.

2.1 President's Address

The current President, Professor Joshua Jortner (Israel) delivered an impressive summary of the current state of the Union. He restated the mission statement and strategic plan which form the basis of the current thorough restructuring and revitalisation of IUPAC.

IUPAC's mission is to advance the world-wide aspects of the chemical sciences and to contribute to the application of chemistry in the service of Mankind. In doing so IUPAC promotes the norms, values and standards of science and advocates the free interchange of scientific information and unimpeded access of scientists to participation in activities related to the chemical sciences.

2.2 Administrative

Secretary-General Dr Becker outlined the achievements of the new Secretariat located at Research Triangle Park, North Carolina under the management of Executive Director Dr John Jost. Administrative efficiencies have seen a lowering of costs and the the IUPAC magazine *Chemistry International* has now achieved profitability. The IUPAC Web site is also fully functional and serving as a centre for administration as well as dissemination of project and other chemical information and links. http://www.iupac.org/

2.3 Decisions Taken by Council and Bureau (my commentary in italics)

Elections

1. Professor P S Steyn (South Africa) was elected Vice President and President Elect.
   The President for 2000-2001 is Dr Alan Hayes (UK). Professor Steyn will succeed in 2002 and is an applied scientist/educationist with strong empathies with southern nations.

2. Dr C Buxtorf (Switzerland) was elected Treasurer.
   John Ward of the UK stood down after an outstanding tenure of 12 years in which he reformed the finances of the Union and he has left it in a very sound position.

3. Dr E D Becker (USA) was re-elected Secretary General. *Dr Becker has been energetic on the restructuring front and has a clear vision of the future for the Union.*

4. Professor N Moreau and Professor O Nefedov (Russia) were elected to the Bureau. Professor H Ohtaki (Japan), and Professor G Schneider (Germany) were re-elected.

Key Council Actions (numbered according to meeting agenda)

1. Approve change to Bylaw 4.307 removing the right for Titular members to receive travel expenses and giving more discretion to the Divisions to allocate financial resources. *Important reform to revitalise commission and project work.*

2. Approved the continuation of all existing Commissions until 2001 under Bylaw 4.302, and their termination after 2001. *See restructuring plans in my GA report.*

3. Approved the Membership and Terms of Reference of the Project Committee and the Evaluation Committee as Standing Committees. *Under the restructuring, the Divisional committees and these standing committees will oversee IUPAC projects and Task Groups.*

6. Approved the appointment of Batchelor, Tillery and Roberts (USA) as the Union's Auditors for 1997-2000. *The old Swiss auditors proved useless!*

7. Approved the Budget and National Subscriptions as proposed by the Treasurer. John Ward presented a very satisfactory budget with an operating surplus for 1998-1999 of US$200k and reserves of US$3.6M. However he called for a small increase in the income from National Subscriptions of 1% to partially compensate for inflation as a matter of principle. New Zealand subscriptions for 2000 and 2001 will be US$2700 and US$2800 respectively (subscriptions are based on chemical industry turnover and New Zealand is 5th lowest of the NAOs). The 2000-2001 budget will put US$550k at the disposal of the Divisions and Standing Committees for project work, an increase of 5%, with further funds possible.

8. Approved the transfer of the Commission on Biotechnology to Division III.

9. Approved the change of the name of Division III to the Division of Organic and Biomolecular Chemistry.

10. Approved the change of the name for those organisations currently known as Observer Countries

to Associate National Adhering Organisations. *Somewhat controversial because OCs do not pay subscriptions but will now receive many of the rights of full NAOs.*

11. Approved the continuation of the Affiliate Membership Program, subject to a biennial report by the Secretary General to Council. *This program has not been an outstanding success except in the US where it has increased the low level of interest in IUPAC.*

12. Approved the dates and location of the 41st General Assembly as 29 June - 8 July 2001, Brisbane, Australia. *To be held in conjunction with the 38th **IUPAC Congress – Frontiers in Chemistry**. The Co-chairs of the Australian organising committee are Professors G George and Robert Gilbert. This is the first IUPAC General Assembly and Congress to be held in the Southern Hemisphere and represents an excellent opportunity for New Zealand chemists to become more involved in IUPAC. The General Assembly and Congress will be more closely integrated than in the past which should facilitate interchanges between researchers and IUPAC project teams.* http://www.ccm.com.au/wcc

13. Approved the dates and location of the 42nd General Assembly and 39th Congress: 8 August - 17 August 2003, Ottawa, Canada.

14/15. Approved the applications of the Turkish Chemical Society and Bulgarian Academy of Sciences for National Adhering Organisation status.

17. Established an IUPAC prize for recent PhDs. There will be up to four prizes per year of US$1,000. The winners for each biennium will also be brought to the IUPAC Congress.

18. Approved a program to provide support of up to US$10,000 for up to two conferences per year in developing and economically disadvantaged countries. *New Zealand?*

19. Approved the change in the National Adhering Organisation for the United Kingdom from the Royal Society to the Royal Society of Chemistry.

Key Bureau Actions

1. Issued a Policy Statement on Continuity in Scientific Activities. *There was great unease from some of the long established IUPAC Commissions and core Working Parties about their imminent abolition. This statement clarified the aims of the reforms (removal of dead wood) and gave reassurance that essential and well regarded Bodies would be reinstated after 2001.*

10. Approved a fund of up to US$25,000, to be matched by the local organisers, to support the participation of scientists from developing and economically disadvantaged countries in the 38th Congress in Brisbane.

11 National Representatives: A Policy Statement - 12 August, 1999. (in full because of implications for New Zealand where National Representatives are our main form of IUPAC representation).

The Bureau has discussed the role of National Representatives, particularly in relation to the integrated program approved by the Bureau in September 1998 to improve the organisation and management of IUPAC's scientific activities. Bylaw 4.305 provides for the nomination and appointment of National Representatives, but defines their role solely by stating that they may attend Commission meetings. In fact, National Representatives participate in a range of activities within Commissions and Standing Committees, particularly the Committee on Teaching of Chemistry. The program approved by the Bureau envisions the termination in 2001 of current Commissions and ultimate reliance on a much smaller number of Commissions, together with a large number of Task Groups formed to carry out specific projects.

One of the aims of the new program is to open participation in IUPAC activities to the worldwide chemistry community. Any individual or group in any country or countries may submit a proposal for an IUPAC project and recommend people to carry out the project. The project-driven system thus has the potential to broaden participation internationally. However, the Bureau believes that each National Adhering Organisation should have assurance that its scientists can participate in the full range of the Union's activities. The program approved last year specified that a limited number of National Representatives may be named to Division Committees, which will become the focus of the scientific activities. Although the size of each Division Committee must remain relatively small in order to carry out its business efficiently, the Bureau believes that some flexibility in numbers of National Representatives should be allowed.

Several National Adhering Organisations have indicated that they would be able and willing to recommend candidates for Task Groups. In addition to such names being considered as part of the core membership of the Task Group, the Bureau believes that each National Adhering Organisation should be able to nominate National Representatives much in the way that they have nominated such Representatives to Commissions. Since each Task Group is to be devoted to a specific project, a National Representative must clearly be qualified and be willing to participate in the project.

The Bureau has adopted the following policies:

A National Representative, as defined in Bylaw 4.305, may be appointed as a non-voting member of a Division Committee on nomination by a National Adhering Organisation and approval by the Division Committee. Normally the number of National Representatives on each Division Committee will be limited to six, but the Executive Committee may approve a larger number if

CONFERENCES & SEMINARS

6-11 February 2000
RACI 11th National Convention
Venue: Canberra, ACT, Australia
Contact: Dr Graeme Moad
Molecular Science, CSIRO
Private Bag 10, Clayton South MDC
Clayton, VIC 3169, Australia
Tel: (+61-3)-95452509
Fax: (+61-3)-95452446
Email: graeme.moad@molsci.csiro.au

14-18 February 2000
ACUN-2 International Composites Meeting - Composites in the Transportation Industry
Venue: University of New South Wales
Sydney, New South Wales, Australia
Contact: Dr Sri Bandyopadhyay
School of Materials Science & Engineering
University of New South Wales
Sydney, NSW 2052, Australia
Tel: (+61-2)-93854509
Fax: (+62-2)-93855956
Email: s.bandyopadhyay@unsw.edu.au

2-5 March 2000
Changing Landscapes, International Landcare 2000
Venue: Melbourne, Australia
Contact: Mandy Bromilow
Tel: (+61-3)-96906744
Fax: (+61-3)-96907155
Email: wscn@bigpond.com
Website: http://www.nre.vic.gov.au/conf/landcare2000/

11-17 March 2000
Xth World Water Conference
Venue: Melbourne, Australia
Contact: Tel: (+61-3)-96820244
Fax: (+61-3)-96820288
Website: http://www.icms.com.au/worldwater

19-23 March 2000
Water 2000 Conference and Expo - "Guarding the Global Resource"
Venue: Auckland, New Zealand
Contact: New Zealand Water and Wastes Association
P O Box 13880
Onehunga, Auckland, New Zealand
Tel: (+64-9)-6363636
Fax: (+64-9)-6361234
Email: water@nzwwa.co.nz
Website: http://www.nzwwa.org.nz

22-25 March 2000
Chain Growth Polymerisation - New Chemistry for the New Millenium
Venue: Santa Rosa, California, USA
Contact: Professor Bruce Novak
University of Massachusetts
Tel: (413)-5452160
Fax: (413)-5450764
or Kris Matyjaszewski
Carnegie Mellon University
Department of Chemistry
Tel: (412)-2683209
Fax: (412)-2686897
Email: km3b@andrew.cmu.edu

2-5 April 2000
Foods - Nutraceuticals - Confectionery - Beverages and Cosmetics
Venue: Doubletree Mission Valley Hotel, San Diego
California, USA
Contact: Mr P C Hereld
Managing Director
The Hereld Organisation
200 Leeder Hill Drive
Hamden CT 06517, USA
Tel/Fax: +1-203-2816766

4-10 April 2000
10th International Conference on High Temperature Materials Chemistry
Venue: Aachen, Germany
Contact: Professor K Hilpert
Forschungszentrum Julich GmbH
Institut fur Werkstoffe der Energietechnik
52425 Julich, Germany
Tel: (+49-2461)-613280
Fax: (+49-2461)-613699
Email: k.hilpert@fz-juelich.de

11-14 April 2000
Food Asia 2000
Venue: Singapore
Contact: Tel: (+65-3)-384747
Fax: (+65-3)-395651
Email: infro@sesmontent.com
Website: www.food.asia.co

21-25 May 2000
10th International IUPAC Symposium on Mycotoxins and Phytotoxins
Venue: Sao Paulo, Brazil
Contact: Dr Myrna Sabino
Instituto Adolfa Lutz
AV Dr Arnaldo 355
Sao Paulo, Brazil, 01246-902
Fax: (+455-11)-8533505
Email: myrna@sti.com.br

1-5 July 2000
13th International Conference on Organic Synthesis
Venue: Warsaw, Poland
Contact: Professor M Chmielewski
Institute of Organic Chemistry
Kasprzaka 44, 01-224 Warsaw 42

P O Box 58, Poland
Tel: (+48-22)-6318788
Fax: (+48-22)-6326681
Email: ichos@ichf.edu.pl

3-6 July 2000
University of Waikato/Amersham Pharmacia Biotech Protein Purification Course
Venue: Hamilton, New Zealand
Contact: R McGowan
Centre for Continuing Education
University of Waikato
Private Bag 3105, Hamilton, New Zealand
Email: rmcgowan@waikato.ac.nz
Website: www.mape.waikato.ac.nz/courses/522htm

9-12 July 2000
Chemeca 2000: Opportunities and Challenges for the Resource and Processing Industries
Venue: Perth, Western Australia
Contact: Conference Secretariat
Chemeca 2000
C/- Congress West Pty Ltd
P O Box 1248
West Perth, WA 6872, Australia

9-14 July 2000
38th International Symposium on Macromolecules
Venue: Warsaw, Poland
Contact: Professor Stanislaw Penczek
Polish Academy of Sciences
ul. Sienkiewicza 112, 90363 Lodz, Poland
Tel: (+48-42)-6819815
Fax: (+48-42)-6847126
Email: spenczek@bilbo.cbmm.lodz.pl

9-14 July 2000
34th International Conference on Coordination Chemistry
Venue: Edinburgh, Scotland, United Kingdom
Contact: Professor P Tasker, Chairman
Dr John F Gibson, Secretary
The Royal Society of Chemistry
Burlington House, London W1V OBN
England, United Kingdom
Tel: (+44-171)-4403321
Fax: (+44-171)-7341227
Email: gibsonj@rsc.org

17-20 July 2000
40th Microsymposium on Polymers In Medicine
Venue: Prague, Czech Republic
Contact: Dr Jaromir Lukas
Institute of Macromolecular Chemistry
Academy of Sciences of the Czech Republic
Heyovskeho na. 2, 162 06 Praha 6
Czech Republic
Tel: (+420-2)-360341
Fax: (+420-2)-367981
Email: sympo@imc.cas.cz

6-11 August 2000
7th International Symposium on Polymer Electrolytes
Venue: Noosa, Queensland, Australia
Contact: Dr Astrid Nordmann
Centre for Advanced Materials Technology
Monash University, Wellington Road
Clayton, Victoria 3168, Australia
Tel: (+61-3)-99055791
Fax: (+61-3)-99054998
Email: ispe7@eng.monash.edu.au
Website: www.chem.monash.edu.au/electrolytes/ispe7

6-11 August 2000
16th IUPAC Conference on Chemical Thermodynamics
Venue: Halifax, Nova Scotia, Canada
Contact: Dr Peter G Kusalik
Department of Chemistry
Dalhousie University
Halifax, Nova Scotia B3H 4J3, Canada
Tel: (+1-902)-4943627
Fax: (+1-902)-4941310
Email: kusalik@is.dal.ca

14-18 August 2000
12th International Conference on Thermal Analysis and Calorimetry
Venue: Copenhagen, Denmark
Contact: Dr O Toft Sorensen
Risoe National Laboratory
Tel: (+45-4)-6775800
Fax: (+45-4)-6775758
Email: o.toft.sorensen@risoe.dk

20-25 August 2000
XIIIth International Congress on Rheology
Venue: Cambridge, England, United Kingdom
Contact: Dr D M Binding
Fax: (+45-1970)-622777
Email: rheology2000@aber.ac.uk

1 September 2000
22nd International Symposium on the Chemistry of Natural Products
Venue: Sao Paulo, Brazil
Contact: Dr M Fatima das G F da Silva
Universidade Federal de Sao Carlos
Depto. de Quimica, Via Washington Luiz
km 235, CP676, Sao Carlos, Brazil
Tel: (+55-16)-2748208
Fax: (+55-16)-2748350
Email: dmfs@power.ufscar.br

3-8 September 2000
11th International Biotechnology Symposium

CONFERENCES & SEMINARS

Venue: Berlin, Germany
Contact: Professor G Kreysa, DECHEMA eV
c/o 11th IBS, Theodor-Heuss-Allee 25
60486 Frankfurt/Main, Germany
Tel: (+49-69)-7564205
Fax: (+49-69)-7564201
Email: info@dechema.de

10-15 September 2000
XXth International Conference on Polyphenols
Venue: Freising-Weihenstephan, Germany
Contact: Professor Dr G Forkmann
Chair of Floriculture and Horticultural Plant Breeding
Technical University Munich
D-85350 Freising-Weihenstephan, Germany
Fax: (+49-81)-61713886
Email: d.treutter@lrz.tum.de

11-14 September 2000
21st International Federation of The Societies of Cosmetic Chemists
Venue: Berlin, Germany
Contact: DGK Secretariat, Konrad-Zirkel-Str 22
D-97769 Bad Bruckenau, Germany
Tel: (+49-9)-7414323
Fax: (+49-9)-7413934
Email: dgk.ev@t-online.de

7-10 October 2000
NZIFST/MIRINZ Joint Conference 2000: Horizons MM! - Designing Foods That Consumers Will Choose
This conference will run concurrently with Xpo's Food Tech 2000, Pack Tech 2000 and the Massey Food Awards.
Contact: Julie Watson
Swift NZ Ltd, P O Box 27056
Mt Roskill, Auckland
Tel: (+64-9)-6256169
Fax: (+64-9)-6256655
Email: jwatson@im.aust.com

8-10 November 2000
2nd International Symposium on Food Packaging - Ensuring the Safety and Quality of Food
Venue: Vienna, Austria
Contact: Dr L Contor
ILSI Europe, 83, Avenue E. Mounier
Box 6, B-1200, Brussels, Belgium
Tel: (+32-2)-7620044
Fax: (+32-2)-7710014
Email: laura@ilsieurope.be

19-22 November 2000
Corrosion & Prevention 2000
Venue: Hyatt Hotel, Auckland
Contact: Corrosion Prevention Centre
P O Box 2340, Mount Waverley
Victoria 3149, Australia
Tel: (+61-3)-98095266
Fax: (+61-3)-98095344
Email: corrprev@internex.com.au

3-8 December 2000
Soil 2000: 2nd Joint New Zealand and Australian Soil Science Societies Conference
Venue: Lincoln University, Canterbury
Contact: Helen Shrewsbury
P O Box 84, Lincoln University
Christchurch, New Zealand
Tel: (+64-3)-3252811 ext 8955
Fax: (+64-3)-3253840
Email: shrewsbh@lincoln.ac.nz

9-13 December 2000
Poly Millenium 2000
Venue: Hilton Waikoloa Village, Waikoloa, Hawaii
Contact: William H Daly
Department of Chemistry
Louisiana State University
Email: bill.daly@chem.lsu.edu

14-19 December 2000
Pacifichem 2000
Venue: Waikiki, Honolulu, Hawaii
Contact: Professor B Halton
Department of Chemistry
Victoria University of Wellington
P O Box 600
Wellington, New Zealand
Fax: (+64-4)-4955241
Email: brian.halton@vuw.ac.nz

26 August - 1 September 2001
XXXIV International Congress of Physiological Sciences
"From Molecule to Malody"
Venue: Christchurch, New Zealand
Contact: The Conference Company
P O Box 90-040, Auckland, New Zealand
Tel: (+64-9)-3601240
Fax: (+64-9)-3601242
Email: info@tcc.co.nz

Dr Tom Learner, Conservation Scientist from the Tate Gallery, London, is presenting a lecture on "**The Analysis of Synthetic Paint Binders**". It will be held at 6 pm on Tuesday 23 November 1999, at the Auckland Art Gallery auditorium. Dr Learner has carried out extensive research into the identification of synthetic resins found in twentieth century artists paint using pyrolysis-gas chromatography-mass spectrometry (pyrolysis GC-MS) and fourier transform-infrared (FT-IR) spectroscopy. For further information please telephone (09) 3077712.

New High Capacity Anion Exchange Column For Polarisable Anions in Complex Sample Matrices

Ai Scientific introduces the Dionex IonPac AS16 column designed for the fast isocratic separation of polarisable anions including thiosulfate, iodide, thiocyanate and perchlorate in a variety of sample matrices. This new method has greatly improved peak shape and efficiency, for polarisable anions, without the use of solvent or other eluent modifiers. The IonPac AS16 is recommended for trace perchlorate in drinking water and ground water matrices. The high-capacity AS16 column allows for the injection of high ionic strength samples without column overload. Using a large loop injection and an isocratic hydroxide eluent, low µg/L (ppb) levels of perchlorate can be determined in less than 10 minutes. The AS16 also provides excellent separation of a variety of other anions including inorganic anions, organic acids and oxyanions. With a hydroxide gradient, 20 inorganic anions and polarisable anions are easily separated in approximately 25 minutes. In addition, highly charged anions including polyphosphates, polycarboxylates and polysulfonates are also readily separated using a hydroxide gradient. The column is available in both 4 mm (standard bore) and 2 mm (microbore) formats and is ideal for use with the Dionex EG40 Eluent Generator, which generates ultrapure hydroxide eluent from water.

Contact: Mark Albertson
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circle number 21 on the reader reply card

Process Analysis In The Near Infrared

The MCS 511 NIR increases the range of Carl Zeiss diode array spectrometer systems with a unit for the near infrared range. This opens up countless possibilities of on-line and at-line process analysis, e.g. in petrochemistry, foodstuff inspection, pharmacy, the life sciences and environmental protection. Its modular design and the wide variety of dedicated measuring heads and software packages, customised on request, make the MCS 511 NIR spectrometer extremely versatile and, in comparison to present systems, very reasonably priced. Its reliability and accuracy are benchmarks in process analysis and quality control.

The centrepiece of the MCS 511 is the MMS NIR, a compact and sturdy spectral sensor consisting of a solid quartz glass body, to which a cross section converter of Infrasil fibres and an InGaAs diode array are permanently connected. It also carries the imaging flat field grating. This technology provides extremely high repeatability for both the wavelength and intensity information. The image corrected and NIR blazed grating, the large aperture and the shape conversion technology result in high light intensity, permitting difficult analytical tasks to be solved.

Depending on the spectral range needed, the MMS NIR module can be equipped with different diode arrays. This gives access to the spectral range from 900 nm to 1.7 µm or 1.4 µm bis 2.2 µm (2.4 µm preparation).

The standard MCS 511 systems include a 16-bit ADC, a serial RS422 interface and 8 digital inputs/outputs. Optional upgrades such as glass fibre data transfer over distances up to 2.5 km, for example, are available, as are different software libraries for controlling the spectrometers and processing the spectral results.

MCS 511 systems can be cascaded via the RS422 interface and be controlled and evaluated by just one PC. This is also possible with other spectrometers of the MCS 500 series, which permits applications in the spectral range of 200-2200 nm to be performed at speeds in the millisecond range. Colours in the visible range and ingredients in the NIR range can be determined with one measurement configuration.

Contact: Carl Zeiss (NZ) Ltd
9-15 Davis Crescent, Newmarket, Auckland
Phone: (09) 5205626, Fax: (09) 5205619
Suite 2, 7 Ward Street, Lower Hutt
Phone: (04) 5667601, Fax: (04) 5667501
Email: info@zeiss.com.au
Website: http://www.zeiss.de
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New Mid-Polarity Chrompack GC/MS Columns Increase Sample Throughput By 10%

Ai Scientific introduces the new Varian/Chrompack CP-Sil 24 CB lowbleed/MS mid-polarity columns. Designed with the latest arylene phase technology, these high-performance columns offer better stability and near zero bleed at elevated temperatures. This translates into less instrument downtime and increases sample throughput by 10%. The Varian/Chrompack CP-Sil 24 CB lowbleed/MS columns provide a wider application range, longer column lifetimes and shorter cycle times with faster column bake out.

Because they are near zero bleed, these columns increase confidence in MS spectral confirmations. Unlike competing columns, Varian has specified a bleed limit for the CP-SIL 24 CB of 6 pA @ 330 °C. The CP-Sil 24 CB columns replace the standard 50% phenyl, 50% dimethylpolysiloxane columns and are ideal for individuals using MS and ion trap MS as well as ECD, NPD, FID and PID detectors.

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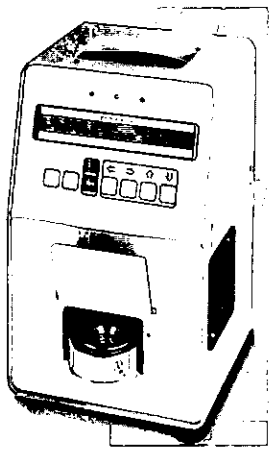
Miniflash Granted ASTM Approval



Ai Scientific is pleased to announce that the Grabner Miniflash closed cup continuous flash point (CCCFP) method has been granted ASTM approval with method number ASTM D 6450. ASTM D 6450 method covers the determination of the flash point of fuel oils, lube oils, solvents and other flammable liquids by a continuously closed cup tester. This flash point test method is a dynamic method and depends on definite rates of temperature increase to control the precision of the test method. The measurement is made on a test specimen of 1 mL, utilising a closed but unsealed cup with air injected into the test chamber. The test method is suitable for testing samples with a flash point from 10 °C to 250 °C. Utilisation of an electric arc, instead of an open flame, combined with the continuously closed cup make the Miniflash the safest automatic flashpoint tester.

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Varian Helps European Laboratories Manage The Belgian Food Crisis

Varian's analytical products are helping European laboratories test for the toxins responsible for the food scare that orginiated in Belgium. Immediately following the initial crisis, Belgium's Ministry of Agriculture and private European food and toxicology laboratories faced significantly increased demand for testing of food samples for contamination. The crisis focused on Belgian meat and dairy products distributed throughout Europe, which were contaminated by two toxic compounds: polychlorinated biphenyls (PCBs) and dioxins. Varian's revolutionary CP-Select PCB 28/31 column, for rapid PCB screening is allowing these laboratories to test for PCBs in half the time of other columns. Once laboratories detect PCBs in food products, they must further test the samples for the cancer-causing chemical dioxin. For this process Varian provided the innovative CP-Sil for Dioxins column. This column offers powerful sample preparation, allowing laboratories to accurately determine precise dioxin levels to establish the severity of contamination.

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New Propac WCX-10 And Propac SCX-10 Columns Separate Proteins That Differ By As Little As A Single Amino Acid Residue

Ai Scientific introduces the new Dionex ProPac WCX-10 and ProPac SCX-10 cation-exchange columns for the analysis of proteins with small differences in charge. The ProPac WCX-10 is a weak cation-exchange column and the ProPac SCX-10 has strong cation-exchange properties. Both columns have unique non-porous pellicular resin design with a very hydrophilic coating that eliminates protein resin hydrophobic interactions. Linker arms containing the cation-exchange functional groups are covalently attached to this hydrophilic coating, making a durable, selective surface. The columns are ideal for characterisation or quality control assays of closely related protein variants. The columns enable scientists in biotechnology, pharmaceutical and food and beverage laboratories to separate and maximise resolution of closely related protein species.

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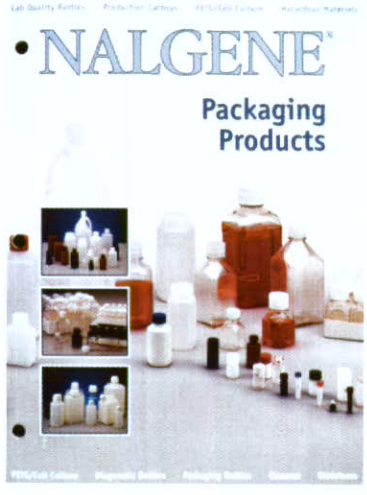
New Nalgene Packaging Products Catalogue Features High Quality Leakproof, Breakproof Containers For Critical Products

Nalge Nunc International Corporation has published a new, comprehensive catalogue of Nalgene Packaging Products for critical applications. Nalgene packaging products are leak-proof, break-proof, and are suitable for packaging or shipment of diagnostic reagents, media, sera, high purity acids or buffers, and are available in a range of sizes from 0.5 mL vials to 50 L carboys.

New Sections:
Cell Culture, Diagnostics, Packaging Bottles, Production Carboys, Biotainers, Hazardous Materials, Lab Quality Bottles, Closures and much more.

Nalge Nunc International, with over 50 years of experience in plastics processing, also offers custom packaging solutions from its ISO9001 and cGMP-qualified facilities.



For a free copy of the new Nalgene Packaging Products Catalogue, visit:
www.nalgenunc.com/packaging. For more information about the full line of Nalgene packaging products,

Contact: NNI Documentation Centre
Sevenoaks, TN 14 5XA, United Kingdom
Fax: (+44-1732)-453166
circle number 27 on the reader reply card

Dionex DX-320 System: Groundbreaking Performance For Ion Chromatography

Ai Scientific introduces the Dionex DX-320 Ion Chromatography (IC) System for high-performance, isocratic IC applications. The DX-320 features superior conductivity detection of analytes present at low-to-high concentrations in a single run, including inorganic anions and cations, ammonia, amines and organic acids. The system provides unparalleled signal-to-noise performance in all applications. These advantages can mainly be attributed to the DX-320's integrated pump and detector, the IC20. The detection technology built into the IC20 features the most advanced conductivity electronics available, while the integrated pump provides a precise eluent delivery system that ensures consistent, reproducible results. Suppressor technology used in the DX-320 complements the high-performance properties of the IC20. The DX-320's Self Regenerating Suppressor (SRS-Ultra) is a high capacity, dynamic suppressor that produces regenerant ions by electrolysis - one of Dionex's patented "Just Add Water" technologies. The SRS-Ultra combined with the EG40 Eluent Generator make IC easier than ever by generating pure eluents on-line using electrolysis of deionised water. Combined with PeakNet Chromatography Software and an AutoSelect AS50 Autosampler the DX-320 meets the greatest demands for increased efficiency and sample throughput. With PeakNet the entire chromatography system - from sample dilution to eluent generation - can be controlled from one software package.

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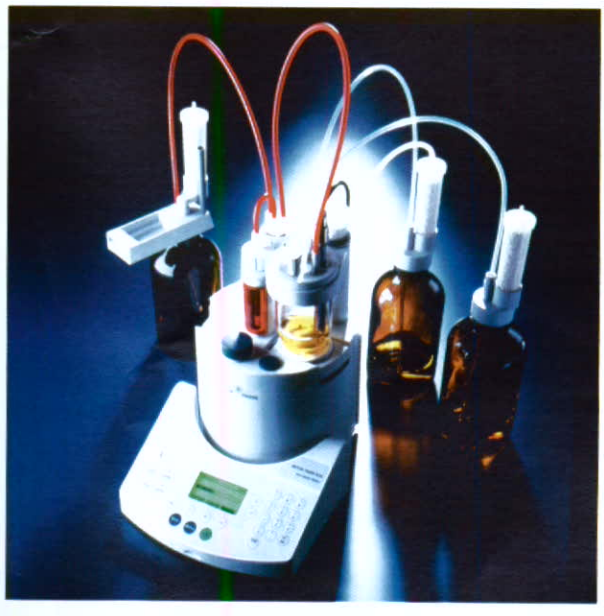
Water Content Determination In New Dialogue



Mettler Toledo has introduced two new innovative titrators which set a new standard in the field of volumetric Karl Fischer titration thanks to their comprehensive dialogue concept supported by a multi-line display and soft keys.

Both KF volumeters incorporate the new <<Hello>> menu, a tutorial which guides the user in dialogue through the installation and method development up to the first titration and thus leads to rapid productivity in daily production. Backup is available through a help program which calculates the optimum amount of sample and provides support by explaining the parameters. Operation is even simpler with the unique <<learn titration>>, which allows the titrator to find the control parameters automatically thereby ensuring that titration methods can be developed faster even by inexperienced users. Although virtually redundant, the compact operating instructions are located in a ready to hand drawer.

The <<fuzzy>> control recently developed by Mettler Toledo for Karl Fischer titration ensures not only rapid and precise determinations, but also flexible adaption to new samples and titrants.

Particular importance has been placed on dependable quality assurance documentation: instrument serial number, batch numbers for standards and titrants and monitoring of their expiry dates are just a few of the features offered.

The simplified DL31 KF Volumeter is suitable for the routine analyst who practically always works with the same titration method, whereas the universal DL38 model is intended for all-round use.

The DL38 contains ten methods pre-programmed and optimised by the manufacturer ready for call up. The soft keys can be used to activate three methods which have priority in every-day work in a particularly simple manner. The DL38 is ideal for determining the bromine number and bromine index; it also calculates water contents in external extractions or external solutions.

It is a simple matter to use the DL38 to control a homogeniser to access moisture in difficult samples. It can evaluate results statistically, tolerances can be entered and their compliance automatically checked. Naturally, the DL38 can also record titration curves.

There is an extensive range of optional equipment and accessories for both KF volumeters, the DLWin PC titration software, the DO305 Drying Oven and the thermostatable vessel are just three examples.

For determinations in the lower ppm range, the DL36 and DL37 Coulometers are available. The extensive product selection from Mettler Toledo for moisture and water content determination also includes halogen and infrared dryers, differential weighing software and thermogravimetric measuring cells.

Contact: John Small, Product Manager
Medic Watson Victor
Free Phone: 0800 508070
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New Propac WCX-10 And Propac SCX-10 Columns Separate Proteins That Differ By As Little As A Single Amino Acid Residue

Ai Scientific introduces the new Dionex ProPac WCX-10 and ProPac SCX-10 cation-exchange columns for the analysis of proteins with small differences in charge. The ProPac WCX-10 is a weak cation-exchange column and the ProPac SCX-10 has strong cation-exchange properties. Both columns have unique non-porous pellicular resin design with a very hydrophilic coating that eliminates protein resin hydrophobic interactions. Linker arms containing the cation-exchange functional groups are covalently attached to this hydrophilic coating, making a durable, selective surface. The columns are ideal for characterisation or quality control assays of closely related protein variants. The columns enable scientists in biotechnology, pharmaceutical and food and beverage laboratories to separate and maximise resolution of closely related protein species.

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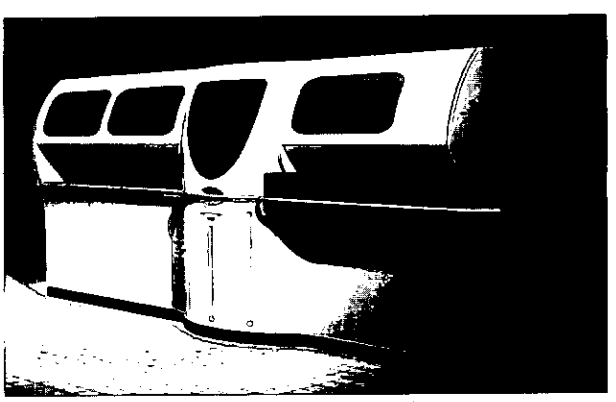
A New Era In Pathology Specimen Management - A.i. Scientific PathFinder Automated Tube Management System



Ai Scientific is proud to announce that Sydney Diagnostic Services (SDS) have ordered the first PathFinder Automated Tube Management System to automate their specimen handling. SDS is one of the largest pathology laboratories in Australasia providing service to the medical profession and patients in the greater Sydney region. Growing pathology workloads had previously been accommodated through automated analysis and management of patient data, now international attention has turned to the automation of specimen handling to improve productivity and to reduce costs, error rates and risk of infection to laboratory staff. With intelligent

software and five independent robots, PathFinder can automatically identify, sort and prepare over 500 blood specimens per hour. PathFinder's hands-free operation removes any potential human error inherent in the manual sorting and splitting of blood specimens. The addition of a PathFinder is representative of SDS's commitment to provide practical and innovative solutions through technology. PathFinder is the result of a four year multi-million dollar design project led by Ai Scientific in cooperation with Leroda Pty Ltd, the Mater Hospital (Brisbane), the Australian Federal Government and Dade Behring Australia. The final PathFinder concept was determined following consultation with a large number of pathology laboratories worldwide. As part of the development process a prototype PathFinder was installed at the Mater Hospital and has successfully processed over 300,000 specimens since mid-1998. PathFinder is currently the only complete system of its type on the international market.

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A Complete New Range Of Sentron ISFET pH Meters And Non-glass, Virtually Unbreakable ISFET pH Probes

SENTRON's Ion Sensitive Field Effect Transistor (ISFET) technology is the most powerful pH testing technology available today. In over 10 years of developing ISFET pH technology SENTRON systems have proved to be reliable, giving good performance in many applications. Based on this experience SENTRON now introduces a completely new and comprehensive range of pH testing equipment, offering capabilities for every application. The new probe range incorporates three series adding up to a total of 10 new probe designs.

Besides a reference system and temperature sensor, these probes incorporate an ISFET as the pH sensing device. Replacing fragile glass electrodes with the sturdy silicon microchip allows for the design of non-glass, virtually unbreakable probes that deliver stable readings in less than 5 seconds. These probes can be used safely in areas where broken glass is a hazard to the user, sample or environment. The patented ElectroStatic Discharge (ESD) protection provides a built-in sensor safeguard.

The new series are:

- The *Red-Line* series of probes, aimed at general purpose applications, where sample temperatures do not exceed 60 °C. The improved design incorporates a non-flow, solid state reference with a large surface area diaphragm of porous PTFE, significantly reducing junction contamination or clogging. This series consists of five different probe designs:

- The *Hot-Line* series a complete new range of high temperature ISFET pH probes, designed for use in demanding applications. These probes incorporate a non-flow, solid state reference with a large area PTFE diaphragm. Using heat and chemical resistant materials as well as high temperature resistant, chemically stable KCl reference gel, these probes function reliably at high temperatures up to 105 °C and in contact with more aggressive chemicals.

- The *Stream-Line* series add a probe design with flow-type reference to the ISFET family. The improved reference incorporates a large surface area diaphragm of porous PTFE and thickened KCl solution. This ensures a constant liquid flow, preventing junction fouling and poisoning, while the diffusion potential is minimised.

SENTRON also introduces a complete new line of ISFET pH meters. Together with the ISFET pH probes these meters form a unique and versatile family of pH measuring systems, offering capabilities for every user's application, environment and data-handling requirements.

This new series of meters, with state-of-the-art electronics and data processing, consists of 4 models in total:

- *The battery powered, waterproof ARGUS and ARGUS c portable meters* are designed to withstand the harshest field, industrial and laboratory environments. They are fully sealed and do not require battery replacement. The real novelty of the advanced *ARGUS* c is *the cradle* that recharges the meter's long life battery pack using a unique, inductive (contactless) method. Data are easily downloaded via an infrared (IR) link between the meter and cradle, then through the cradle's RS232 port to computer or printer. There are no external contacts on the *ARGUS* c ensuring an IP67 (fully waterproof) rating.

- *The both mains and battery powered TITAN and TITAN c benchtop meters* are ideally suited for laboratory use as well as for remote-site measurements. Incorporating the best available features and state-of-the-art technology, this series offers sophisticated signal processing and data handling facilities. The advanced *TITAN* c benchtop meter is equipped with programmable high and low pH alarms, indicated on the display and by an acoustic signal and/or by relay contact outputs. This model also incorporates an analogue mV output for real-time, continuous data recording.

All instruments display pH and temperature on a clear multi-functional LCD graphics display. The adjustable contrast makes reading in any light easy, while the backlit

display of the advanced *TITAN* c and *ARGUS* c allow reading in darker environments. The meters offer data storage facilities for up to 300 measurement data points, including date and time. Results can be recalled onto the display and uploaded to a computer or printer via a serial RS232 output. Start, Interval and total duration times are user programmable as is the flexible 9-digit sample ID. Automatic Temperature Compensation (ATC) ensures reliable calibration and measurement results at any temperature. User-programmable calibration prompts on the advanced models remind the user when it is time to recalibrate.

Performance of meters and probes is continually monitored, supported by a comprehensive set of self-diagnostic functions. A probe recognition function ensures that the system has been calibrated with the probe in use. Every calibration is monitored resulting in an updated display of probe status allowing an estimation of its remaining life.

The advanced "*c*" models satisfy all requirements of Good Laboratory Practice (GLP).

Contact: Total Lab Systems Ltd
P O Box 29071, Greenwoods Corner, Auckland
Phone: (09) 6252570, Fax: (09) 6252572
Email: sales@totallab.co.nz
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- *The chromatographer wants to get a sample chromatogram for a new column he/she is thinking of using.*

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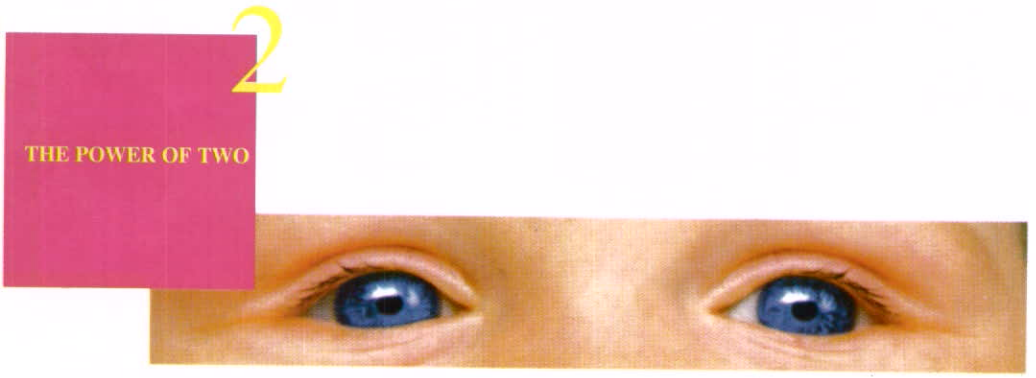

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