

CURRENT PATENTS GAZETTE



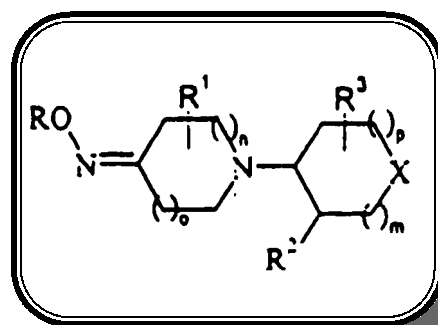
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DRUG PATENTING IN CONTEXT

Current Patents *Gazette* is the most rapid competitive intelligence service covering innovation in the pharmaceutical industry. Patent applications published during the past week have been classified and analysed, in order to place the inventions in context. For the most crucial innovations, those involving new chemical compounds, additional information is given in the form of front page images. These can be enlarged to show details of chemical structures and inventor teams, for example. Applications filed jointly, representing collaborative research, are highlighted, as are sequences of inter-related documents.

Among 14 new applications from Alcon we see claims to new oximino- and phthalimide substituted piperidine, pyrrolidine and azepines and claiming their use as muscarinic agents for treatment of glaucoma, myopia and other conditions.



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HIGHLIGHTS THIS WEEK

It has been a highly productive week for Alcon Laboratories with no less than **14 new applications** published and covered within the pages of this issue of the *Gazette*. Among this week's New Compounds there are six cases referring to new **oximino-** and **phthalimide substituted piperidine, pyrrolidine and azepines** and claiming their use as **muscarinic agents** for treatment of **glaucoma, myopia** and other conditions. This appears to be a new mode of attack for Alcon, but **Merck, Lilly, Sandoz** and **Novo Nordisk** have all previously reported the approach. Alcon's glaucoma treatments have seem to have concentrated on the use of prostaglandins and their analogs, and this more traditional approach can be seen among this week's New Formulation and Use cases. Also in Section B, we see eight more disclosures from the company including three describing the treatment of **GLC1A glaucoma** with (non-steroidal) **glucocorticoid antagonists** and **angiostatic agents**. Claims to the use of **benzofurans** and **benzopyrans** as **cytoprotective agents, aminobiguanides** for disinfecting contact lenses and **brinzolamide**, a carbonic anhydrase inhibitor launched for glaucoma, to prevent visual field loss are also evident.

An application from Lilly published this week is claims **l-lipotropin** and its uses in the treatment of **diabetes** and associated complications. Research in this area is very topical at the moment. Lilly's insulin analog, **insulin lispro**, an ornithine-decarboxylase stimulator, was first approved by the EU in May 1996 and has now been extensively launched. Diabetes is popular target for work at Lilly, and has resulted in several collaborations, including the **Garvan Institute for Medical Research** to develop and market treatments for diabetes, and with **Boehringer Mannheim** to develop a program to deliver diabetes care worldwide. Another important collaboration for Lilly is with **Dura Pharmaceuticals**; they are investigating insulin delivered via Dura's **Spiros inhalant delivery system** for the potential treatment of insulin-dependent diabetes.

As we pointed out in the last issue, hardly a week passes without new filings on the **synthesis of taxanes**. This week is no exception with an application from the Canadian company **BCM Development Inc**. However, this time we are also reminded by two applications about the preparation of **carbocyclic nucleosides**, such as **carbovir** or **abacavir**, of another important class of compounds for pharmaceutical chemists. Researchers from the Japanese company **Kuraray** have invented a highly efficient one-step process for producing **2-azabicyclo[2.2.1]hept-en-3-one** in high yield and potentially on a large scale from alkyl- or phenyl-substituted sulfonyl cyanide. This compound is commonly used for the preparation of **4-aminocyclopent-2-en-1-methanol** or its 2,3-dihydroxy derivative. These substances can be used to form the carbocyclic part of the aforementioned nucleosides. Some might think that an improved method for producing the azabicycloheptenone does not constitute a great leap forward in the synthesis of carbocyclic nucleosides, not least because of the difficulty of its conversion to the cyclopentene analog but consideration of an new application **Lonza** may change their minds. Probably based on a co-operation agreement with **Glaxo Wellcome**, it claims a simple and cost-effective method for the reduction of azabicyclohepten to 4-aminocyclopent-2-en-1-methanol, and also includes a method of processing it further to a pyrimidine-based nucleotide, a key intermediate for Glaxo's recently launched HIV reverse transcriptase inhibitor abacavir.

A joint application from the Interneuron subsidiary Progenitor and Vanderbilt University focuses on a lipase expressed in endothelial cells. Suggested uses for the disclosed polypeptides and polynucleotides include the diagnosis and treatment of vascular disorders, lipidemia, diabetes and obesity. These topics appear popular at Progenitor, with the USPTO issuing two patents covering the **leptin receptor**: US5763211 and US5643748. As of June 1998, the company also had exclusive rights for certain uses of the leptin receptor such as screening and selection of small molecules that bind to it, blocking its function or mimicking its activities. Progenitor's partnership with Vanderbilt Univ has been a fruitful one too, leading to the discovery of the **developmental endothelial locus-1 (del-1) gene** (EP854883). The encoded protein, Del-1, is a cell surface protein involved in the growth and development of bone and blood vessels. In April 1999, **Megabios** acquired rights to this gene, and is investigating it for cardiovascular indications.