

CURRENT PATENTS GAZETTE



current-science.com

ISSN 1464-3499

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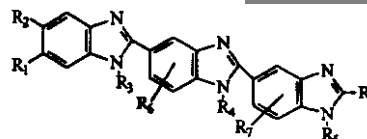
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DRUG PATENTING IN CONTEXT

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.

NEW THIS WEEK

Rutgers University publishes another in a recent series of trisbenzimidazole based topoisomerase inhibitors related to JSKIV-47.



HIGHLIGHTS THIS WEEK

From India there are only a few dozen international patent applications each year relating to pharmaceuticals, and by far the most prolific applicant is **Dr Reddy's Research Foundation**, which has US links. However, **Ranbaxy Laboratories** of New Delhi is also in the habit of filing applications outside India, and has now accumulated more than a dozen US patents relating to the production of generic versions of established products. In the most recent, further synthetic routes to the successful **HMG-CoA reductase inhibitors lovastatin** and **simvastatin** are claimed. Many of the earlier patented Ranbaxy processes were for anti-infectives (**penicillins, cephalosporins and tetracyclines**), but there were also inventions concerned with **midazolam** and **ranitidine**. It has only recently become possible validly to claim priority from an Indian application when filing elsewhere; of fewer than a hundred US patents claiming Indian priorities, the majority are biomedical in nature.

Whereas Ranbaxy's interest in manufacturing other companies' compounds is confined to products nearing patent expiry, **Kuraray** is seeking protection relevant to a **Merck** product launched only at the end of 1998. The claimed cyclopropylacetylenes are side-chains for the benzoxazinone **efavirenz**, though the application was filed well before the product's launch, and indeed the target compound is referred to by means of its preclinical research code. Kuraray has no compound of this type in development, and no reported direct interest in efavirenz, which Merck claimed in EP582455. In contrast, it is not at all surprising to see the two PCT applications in the name of **DuPont** claiming **oral liquid formulations** of benzoxazinone HIV RTIs; efavirenz is a product of the **DuPont Merck** collaboration, now formally terminated but still in evidence as joint marketing arrangements.

Pfizer reports progress in the development of **matrix metalloproteinase inhibitors** suitable for treatment of osteoarthritis. However, new compounds seem not to be involved. Rather, the claims are to the use of agents which selectively inhibit **MMP-13 (collagenase-3)** versus MMP-1, an idea apparently introduced but not necessarily demonstrated in EP780386, an application in the names of **Roche** and **Agouron**. In this context Pfizer workers have already reported a study of **phosphinates** which bind specifically to the **S2 pocket** of the enzymes, and two of the agents named in the present claims are of the same type. Another MMP inhibitor specialist, **British Biotech**, is claiming the use of **anti-inflammatory hydroxamic acids**, compounds in the same class and from the same team as the phase III candidate marimastat. On this occasion, however, the compounds are described as **inhibitors of intracellular leukotriene A4 hydrolase** activity. **Santen, Searle** and **RPR** are among the small number of companies exploring this specific anti-inflammatory mechanism.

RPR has brought together a team from France, Belgium, Italy and Morocco to study the use of **selenium compounds in Alzheimer's disease**. This work is not entirely without precedent, in the sense that the RPR subsidiary **Nattermann** originated **ebesen**, and has already described its use in Alzheimer's disease in WO9808511. Selenium compounds are recognized antioxidants, and have also featured in cases such as EP804927, in which **Pharma Nord** incorporates **L-selenomethionine** in an **antioxidant** composition for which Alzheimer's disease is one of the indications. Two members of the present RPR team contributed to a paper on this subject given at the 28th Annual Meeting of the Society for Neuroscience in November 1998. The compounds now being claimed do not initially appear to be related to **ebesen**, but the benzamide structures with a selenoether substituent in the 2-position are ones which could clearly be cyclized to a **benzisoselenazole**, and they are plausible **metabolites of ebesen**.