OVER VIEW

A new era is dawning in drug research. New ways of developing better and safer drugs are becoming apparent. Major changes are taking place both in how and which chemical compounds are tested for their therapeutic usefulness and in the possibilities for interpreting biological effects at the molecular level.

This new era has arisen partly from the exciting advances in the scientific knowledge of the molecular basis of bodily functions and of how these functions change in illness.

Technological innovations, particularly in fields of molecular and structural biology and computer technology are making significant contributions to modern drug research.

Furthermore the substantial advances in the capabilities of theoretical and synthetic chemistry, as well as macromolecular structure determination by X-ray diffraction and NMR-spectroscopy have led to an increasing understanding of the interactions of active compounds with their biological target molecules. Because of the progress in all the fields it is now sometimes possible to study in atomic details, the binding sites for ligands on DNA, enzymes and other proteins such as antibodies. In such cases, the variation of the affinity within a series of test compounds can be interpreted.
in the light of how the individual molecules fit into the macromolecular binding site.

The most dramatic advance of modern biology is undoubtedly that of genetic engineering. With these techniques scientists can now produce large quantities of specific DNA, RNA or protein molecules; molecules that form the structural and functional basis of living things. Furthermore, specific changes can be made to these molecules to probe the effect of such changes in structure, on changes in function. As a consequence of these and related development in biochemistry, strategies and experimental methods used in the search for new drugs are changing fundamentally, where once testing of potential new drugs started with studies in organ or whole animal preparations. Such tests are now secondary to biochemical tests.

Technological advances in problems, on the other hand, provide a vital basis for innovations in pharmaceutical dosage forms that are safer and more convenient for the patient or that expand the types of molecules suitable for therapeutic use.

However, it is not only scientific and technical developments that are changing the face of drug research; the research and development environment at pharmaceutical companies has also experienced change. Special disciplines no longer stand alone as independent units; research and development processes now center around collaboration within interdisciplinary project groups.
Better and safer drugs will be discovered and developed by close collaboration of pharmacologists, biochemists, molecular biologists, medicinal and theoretical chemists, toxicologists, pharmacists and physicians.

Considering all the means that have been made available for modern drug design, one wonders why medicinal chemists in former times were so admirably successful and why progress in drug therapy appears so slow now a days. Certainly, the demands put on new drugs are much higher now a days than they were in former times. Also the problems that still challenge (e.g., NSAIDs, Cancer, AIDS, autoimmune diseases, dementia etc.) are much harder to tackle, otherwise at least some of them would have been solved already. Yet this alone does not explain why such remarkable progress was possible in the early stages of medicinal chemistry. Probably it was the intuition, the creative potential and an open mindedness that made the old chemists so successful, without our modem tools. These virtues must be encouraged because still today it is the medicinal chemist's creative potential and openness for new principles and concepts that we ultimately determine as the progress in drug therapy. Therefore, we should not let ourselves be misled by the computer into worrying about significant details and into seeking perfectionist solutions. The human intuition should also be given due importance.

In view of these general observations and established pharmacological activities of 1,2,4-triazoles, 1,3,4-oxadiazoles, 1,3-thiazolidin-4-ones and azetidin-2-ones which include antibacterial, antiinflammatory,
anticonvulsant, anticancer, antihypertensive, diuretic and analgesic activities, it was thought to synthesise and investigate compounds with comparable structure for their antiinflammatory, analgesic, antimicrobial and antituberculosis activities. Thus, the basis of the present investigation was centered around the fact that certain structural units present in biologically active compounds are also found in other compounds of similar properties. Thus by effecting structural variations and modifying molecular structure, biological activity could be better innovated e.g., by introducing the heterocyclic moieties such as 1,2,4-triazoles, 1,3,4-oxadiazoles, 1,3,4-thiadiazoles Boschelli et. al.,2 achieved the enhancement of the antiinflammatory activity of the phenamate derivatives to a greater extent. They were successful in reducing their ulcerogenicity as well. According to authors, increase in the antiinflammatory activity and the reduction in the ulcerogenicity is due to the selective inhibition of 5-lipooxygenase (5-LO), cyclooxygenase (CO) and thereby blocking the biosynthesis of prostaglandins and leukotrienes, the proinflammatories and promoters of gastric ulceration respectively.

So the net conclusion is modern medicinal chemists still need luck to a certain extent and luck does not favour the computer, but the prepared (open) mind.

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