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Formulation of Macrocyclic Molecules for Pharmaceutical Use

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Commentary

In organic synthesis, biochemistry, and medicine, finding novel biologically active chemicals to address global health concerns is a critical objective. The biological activity of macrocyclic structures is a field of research that is still in its early stages. Macrocyclic compounds feature distinct physicochemical characteristics, such as spatial preorganization, the existence of a size-defined cavity, the proclivity for self-assembly, low pharmacologically active doses, low toxicity, and antiallergenicity. Crown ethers, cyclodextrins, cucurbiturils, calixarenes, porphyrins, pillararenes, and cyclic peptides are examples of macrocyclic molecules that have been employed in biological applications.

The usage of macrocycle-antibiotic hybrids is one technique to combat microorganism antimicrobial resistance. It describes the production and characteristics of the most well-known macrocyclic compound-antibiotic hybrids, such as rifamycins, vancomycin, and others. The increase in molecular weight is acknowledged to be one of the key drawbacks of using antibiotic hybrids. However, research and advancements in this domain suggest that bulky compounds' oral bioavailability for systemic therapeutic usage can be improved.

Novel Tröger's base derivatives have been produced and their anticancer characteristics explored by several researchers. The anticancer efficacy of Tröger's base phenhomazines derivatives was tested, and 1,4,7,10-tetraoxa[10](2,8) trögerophane showed good selectivity on a colon cell line, with an IC50 of 92.7 g/ml. The findings suggest that new potential anticancer drugs might be developed as a result of the findings.

It is well known that macrocyclic compounds can be employed as drug containers in targeted delivery systems. Cucurbit[7]uril has been demonstrated to form a host-guest combination with the neurotransmitter serotonin. The binding affinity is pH-dependent in this scenario. The findings show that serotonin delivery and pH-controlled release have biological uses. Cucurbit[7]uril has been used as a liver protecting agent and adjuvant in toxicological pharmacology. Cucurbit[7]uril's protective properties were tested in a biochemical research of mice's extracted livers after cyanobacterial crude extract therapy with or without cucurbit[7]uril. *In-vivo*, the addition of cucurbit[7]uril dramatically reduced the toxicity of cyanotoxin-induced hepatotoxicity (p=0.05).

Supramolecular chemistry can be used to administer immunomodulatory medicines in a regulated and/or localized manner. In several publications, macrocycles like cyclodextrins are highlighted for their drug solubilizing and stabilizing properties, as well as the use of polymer-based hydrogels and nanomaterial’s for local drug delivery. Apart from drug transport, cyclodextrin-based supramolecular systems have found uses in biomedical fields such as biomolecule separation, enzymatic catalysis, sensing, diagnostics, and treatment. The chirality of cyclodextrins makes them ideal for biomolecule separation. According to the molecular mechanics simulation, even a low-cost native cyclodextrin like -cyclodextrin can distinguish between the enantiomer forms of the amino acids alanine, valine, leucine, and isoleucine.

The advancement of macrocyclic chemistry has aided in the creation of novel catalytic materials that are both effective and selective. Advances in the utilization of macrocyclic molecules as building blocks for the construction of bio inspired catalysts have been documented by several researchers. From single molecules to metal-organic framework materials, the presented materials show unique catalytic characteristics and binding affinity for physiologically important substrates. At this

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point of study, the researchers concur that the materials developed have lesser catalytic activity than natural enzymes. However, the current trend in synthetic catalyst research may lead to future applications.

Ion transport across lipid bilayers is an essential supramolecular activity with potential uses in biophysics research and ion channel disorder therapy. Macrocyclic ionophores are of special importance for obtaining high membrane transport selectivity, as demonstrated by the natural product valinomycin's nearly complete K+ over Na+ selectivity. Some researchers have produced a cyclic azapeptide anionophore with a tiny binding pocket that allows fluoride ions to be transported selectively through membranes. Surprisingly, this anionophore transports bigger anions like chloride and acetate rather poorly.