Prodrugs and Soft Drugs

Previously we have shown that fatty acid extract from fish-liver oil does possess some antibacterial activity. We have investigated how these fatty acids and related compounds, can be used as pro-moieties in prodrug design and as building blocks for soft drugs.

Prodrugs

Prodrugs are pharmacologically inactive derivatives of active drugs. They are designed to maximize the amount of active drug that reaches its site of action, through manipulation of the physicochemical, biopharmaceutical or pharmacokinetic properties of the drug. Prodrugs are converted into the active drug within the body through enzymatic or non-enzymatic reactions.

Some publications

T. Thorsteinsson, M. Másson, T. Järvinen, T. Nevalainen and T. Loftsson, „Cycloserine fatty acid derivatives as prodrugs: Synthesis, degradation and in vitro skin permeability", *Chem. Pharm. Bull.* **50**, 554-557 (2002).

M. Másson, T. Loftsson and G.G. Haraldsson, „Marine lipids for prodrugs, soft compounds and other pharmaceutical applications", *Pharmazie*, **55**, 172-177 (2000).

M. Másson, T. Thorsteinsson, T. H. Sigurðsson and T. Loftsson, „Lipophilic metronidazole derivatives and their absorption through hairless mouse skin", *Pharmazie*, 55, 369-371 (2000).

T. Thorsteinsson, M. Masson and T. Loftsson, „Dermal delivery of ETH-615, a zwitterionic drug", *Drug Devel. Ind. Pharm.* 26, 709-714 (2000).

T. Thorsteinsson, M. Másson, T. Loftsson, G.G. Haraldsson and E. Stefánsson, „Diacyl glyceryl ester prodrugs for slow release in the skin: synthesis and in vitro degradation and absorption studies for naproxen derivatives", *Pharmazie*, 54, 831-836 (1999).

Soft drugs

Drugs are sometimes divided into "hard drugs " and "soft drugs". Hard drugs are "non-metabolizable drugs" or drugs which are metabolized to biologically active metabolites. The metabolites of hard drugs are frequently toxic oxidation products. Soft drugs are drugs which are characterized by a predictable and controllable in vivo destruction (i.e. metabolism) to non-toxic products after they have achieved their therapeutic role. Similarly "hard compounds" can be defined as compounds which do not degrade in the environment or compounds which do it very slowly. Thus, these compounds will lead to progressive pollution of the environment. An example of a hard compound is the insecticide DDT. "Soft compounds" can be defined as biologically active compounds which are readily degraded to non-toxic and biologically inactive degradation products in the environment. The purpose of this project is to design, synthesise and test soft drugs and soft environmental-friendly compounds.

Some publications

T. Loftsson, T. Thorsteinsson and M. Másson, „Marine lipids as building blocks for soft quaternary ammonium compounds and their antibacterial activity", *Pharmazie* (in print).

T. Thorsteinsson, M. Másson, K. G. Kristinsson, M. A. Hjálmarsdóttir, H. Hilmarsson and T. Loftsson, „Soft antimicrobial agents: synthesis and activity of labile environmental friendly long chain quaternary ammonium compounds", *J. Med. Chem.*, **46**, 4173-4181 (2003).

T. Thorsteinsson, T. Loftsson and M. Masson, „Soft antibacterial agents", *Current medicinal Chemistry*, **10**, 1241-1253 (2003).

R. J. Little, N. Bodor and T. Loftsson, „Soft drugs based on hydrocortisone. The inactive metabolite approach and its application to steroidal antiinflammatory agents", *Pharm. Res.* 16, 961-967 (1999).