## Bioactive Ether Lipids
## Synthesis and Biological Activity

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Alkyl lysophospholipid (ALP) analogs have received much interest in recent years because of their cytotoxic effects on malignant cells *in vitro* and *in vivo*. Although the mechanism of action of ALPs still remains to be elucidated, these agents do not affect nuclear DNA and are not genotoxic. Their major target sites appear to be in the plasma membrane.

Structure activity relationship studies on a variety of alkyllysophosphocholines showed that a long alkyl chain and a phosphocholine moiety represent the minimal stuctural requirements for antineoplastic activity of ALPs. Hexadecylphosphocholine HePC (Miltefosine) represents the first anticancer agent which was specifically formulated for the topical, palliative treatment of skin metastases in patients with breast cancer. Its therapeutic potential in further indications, such as cutaneous forms of leishmaniasis and skin cancer is being clinically tested.

In order to probe the structural and stereochemical requirements of amphipathic ether lipids for optimal cytotoxicity and/or immunomodulation we have synthesized a variety of analogs containing different head groups and lipid portions. The head group contains several substituted amines while the lipid portion encompasses long aliphatic or alkoxyethyl chains or suitably substituted aryloxyethyl moieties.

The cytotoxic activity of the new compounds was evaluated *in vitro* against a panel of six human tumor xenografts and in two biochemical, mechanism based, screens. In addition, data on the fungistatic and fungicidal activity, as well as the parasiticidal action against the amastigotes *Leishmania donovani* and *Leishmania tropica*, of the new alkyllysophospholipids, will be presented.

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