

## Design and synthesis of ibuprofen salts as anti-inflammatory agents in the form of semi-solid preparations for topical use

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Roschlaw et al (1985) demonstrated that the arylacetic acid derivatives are preferred for long-term use for the treatment of inflammatory disorders, including rheumatic disease, osteoarthritis, and ankylosing spondylitis. However these compounds are generally highly protein-bound drugs, including very high binding to tissue proteins (Belousov et al 1997). Their metabolism is extensive and they are also partly biliary excreted. Because of these properties, the commonly used therapeutic doses need to be relatively high, often up to 600 mg, with the attendant tendency to adverse effects, particularly with regard to gastrointestinal effects. This may limit the use of these drugs orally and creams, gels and ointments have been developed for topical use.

The aim of our research was to prepare appropriate salts of ibuprofen which would have improved bioavailability when given orally and to develop topical formulations with improved skin permeation.

We have studied sixteen different hydrophilic and diphilic compositions for topical use, containing water or water-soluble vehicles, co-solvents (DMSO) and surface-active ingredients (polysorbate-80, span-60 and others).

Stability was assessed by quantitative spectrophotometric analysis for the active drug component

( $\lambda_{\max}$  = 264 nm; relative error 1.28%), pH range (5.94–7.15, according to the nature of the vehicle). Melting points of the prepared ointments lay within the range 36.4 to 37°C and the acidity of the diphilic vehicles was between 2.0 and 2.5. The dynamic viscosity of the ointments was investigated using Reotest 2 and the range of this value under 12 speed parameters was from 37.8 to 0.9 Pa s. Anti-inflammatory activity was assessed by the rat-paw oedema assay (Trinus et al 1975).

Sodium and potassium salts of ibuprofen were stable in hydrophilic vehicles, and calcium salts were stable in both hydrophilic and diphilic (w/o) vehicles.

Our results showed that ibuprofen sodium, potassium and calcium salts can be used in the form of ointments, containing hydrophilic vehicles (macrogol) with a co-solvent (DMSO) and a surface-active agent (polysorbate-80).

Belousov et al (1997) In: Guidelines for Physicians, Univer-sum Publishing, Moscow, 215–233 (in Russian)

Trinus Ph. P. et al (1975) In: Non-steroidal anti-inflammatory drugs, Zdorov'ya, Kyiv, 239 (in Russian)

Walter H. E. (1985) In: Principles of Medical Pharmacology, 4th edn, Toronto, pp394–395