

Wissenschaftliche Posterausstellung: Poster 10

An innovative vehicle based on lyotropic formulations containing up to 20 % diclofenac for combating local peripheral pain

Doris Barnikol-Keuten, W. Barnikol and L. Köhler

Privatärztliche Ambulanz für chronische Wunden und lokale Schmerzen, Hilgestr. 24, 55294 Bodenheim bei Mainz

The problem

Combating local peripheral pain by a systemic therapy is often contra-indicated or even impossible, because of serious comorbidities of the patients. In addition systemic pain therapy often fails, because the local level of effectiveness cannot be reached because the therapeutic quotient of the pain drug employed is too low.

But in many cases also the local therapy fails, because of too a low skin permeation of the applied formulation, so that the local effective concentration of the drug cannot be achieved.

The new vehicle

Three main components constitute the new vehicle.

First, a lyotropic fluid based on nonionic tensides. These fluids have two very interesting properties: they are very good solvents for all kinds of substances (drugs): hydrophilic, lipophilic, amphiphilic and they render possible a good permeation through the horny layer of the skin.

Second, the new vehicle contains capsaicin, which opens the cutaneous vessels to the maximum. This increases the skin perfusion and so the drug transport to the inner tissues. Also it empties the substance P stores, combating the second pain of capsaicin very effectively, but capsaicin generates a strong first pain.

Third, to cut off this first pain, the vehicle contains also lidocain.

The formulations

In order to combat local pain with the new vehicle, we have chosen diclofenac as pain drug. Two special formulations were developed: DoloCur for the hairless skin of men and HippoCur for the haired skin, especially for horses. The first formulation contains 20% diclofenac, the second 15%. In hairless skin mainly the intercellular permeation is working, whereas in haired skin additionally there is working the transfollicular penetration mechanism.

The formulations are colourless clear gelic fluids and at least stable for 2 years.

The application

The standard application procedure comprises 7 applications daily in the first week and 7 applications every second day in the following fortnight. In case of hairless skin (DoloCur) 10 drops are rubbed into 100 cm² skin, taking 2 fingers protected with a cot. 1 drop taken from an injection needle weighs 25mg and contains 5mg diclofenac. In case of haired skin 1g of HippoCur (i.e. 150mg diclofenac) are sprayed onto the skin parallel to the hair around the carpal joint of a horse.

Results

1) Dynamic light scattering (DLS) investigation:



The results of both formulations are different: HippoCur has 2 maxima at 45 and 340 nm, DoloCur at 15 and 89 nm. Both preparations show polydispersity and low signals.

2) Drug levels in the carpal joints of horses:

Five horses were treated with HippoCur as described above. After treatment synovial fluid was taken from the joints and analysed for diclofenac, at the same time the blood plasma of the animals was analysed (the analysis was done with HPLC combined with mass spectrometry for detection). The average value for diclofenac level in the synovial fluids was 210 ± 5 ng/ml (mean \pm SD, n= 5). Diclofenac could not be detected and measured in blood plasma, the content was under the limit of proof, which is 3 ng/ml.

3) Clinical case series in horses with HippoCur:

In 94 horses with different orthopedic indications concerning the limbs of the animals HippoCur was applied as described. The quote of clinical success (abolishing laming) was found to be 90%.

4) Clinical case series in men with DoloCur:

In men (more than 100 cases) with different indications like heel spur or CRPS (complex regional pain syndrome) or tendinosis the average quote of clinical success (abolishing pain) was 75%. No case of skin irritation was observed.

Discussion

The results of the light scattering investigations indicate the existence of mesophases within the formulations.

It is clear from the description of the procedure that the treatment is the more successful the nearer the locus of pain lies to the skin surface. We estimate the deepness of effectivity to be about 2cm, because it was possible to treat successfully also a man's wrist.

The effective tissue level of diclofenac is discussed thoroughly by Chlud and Wagner [1]. The authors regarding synovial fluid come to the effective range of 100-500ng/ml for diclofenac. It is seen that the effective diclofenac levels, achieved in the investigations reported here, lies well within this range.

Kriwet und Müller-Goymann have shown, that diclofenac itself is mesogenic in diethylamine water system [2].

The new vehicle may also be used for formulations with other drugs, because the vehicle is universal.

References

[1] Chlud K, Wagner HH

Perkutane Therapie mit NSAID (NON-Steroidal Anti-Inflammatory Drugs) unter besonderer Berücksichtigung kinetischer Fragen
EULAR Bulletin 2 (1987) 41-45

[2] Kriwet K, Müller-Goymann CC

Binary diclofenac diethylamine water systems: micelles, vesicles, and lyotropic liquid crystals
Eur J Pharm Biopharm 39 (1993) 234-238

Fon 0049173-2113433

E-address barnikolwolfgang@hotmail.de

