嘉南藥理科技大學專題研究計畫成果報告

計畫名稱

Transdermal delivery of nalbuphine and sebacoyl dinalbuphine ester

計畫類別：個別型計畫

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The major aim of this study is to assess the transdermal permeation characteristics of nalbuphine and its novel prodrug- sebacoyl dinalbuphine ester.　Nalbuphine is a narcotic analgesic used in the treatment of both acute and chronic pain.　Due to its short elimination half-life and bioavailability, a series of nalbuphine prodrugs have been synthesized.　Since the transdermal permeation characteristics are different for drugs with various physicochemical properties, the permeation rates of nalbuphine and sebacoyl dinalbuphine ester can be significantly different.　Therefore, in order to achieve systemic delivery of nabuphine and its prodrugs via skin route, it is necessary to characterize their permeation characteristics in a systematic way.　In this study, their permeation through nude mouse skin will be evaluated using horizontal glass diffusion cells. The permeation data will be analyzed to assess the effects of physicochemical properties on the permeation properties for nalbuphine and sebacoyl dinalbuphine ester.

The results (Figure) indicate that the application of iontophoresis and electroporation as well as simultaneously application of both driving forces may enhance the transdermal permeation of nalbuphine (NA), nalbuphine benzoate ester (NAB) and sebacoyl nalbuphine (SDN).　The

application of various molecular weight of HPC gel also have influence on the permeation of nalbuphine and its prodrugs (Table).

Table . The flux ($\mu g/cm^2/h$) of nalbuphine and its prodrugs from HPC hydrogels with low and high molecular weight (MW)

Condition	Compound	High MW HPC	Low MW HPC
Passive diffusion	Nalbuphine	0.16±0.04	0.32±0.07
	N. Benzoate	0.36±0.05	0.35±0.06
	Dinalbuphine	0	0
Iontophoresis+Electroporation	Nalbuphine	20.50±1.73	30.55±3.56
	N. Benzoate	19.00±4.09	24.25 ±5.66
	Dinalbuphine	4.83±0.43	5.17±1.32

(A) NA

Flux (μg/cm^2/h)

● Passive	0.33±0.06
○ Iontophoresis	8.64±4.62
▼ Electroporation	3.90±0.53
▽ Combination	34.63±5.28

Cumulative amount (μg/cm^2)

Time (h)

(B) NAB

Flux (μg/cm^2/h)

● Passive	0.48±0.07
○ Iontophoresis	20.08±2.77
▼ Electroporation	1.39±0.49
▽ Combination	18.84±0.58

Cumulative amount (μg/cm^2)

Time (h)

(C) SDN

Flux (μg/cm^2/h)

● Passive	0±0
○ Iontophoresis	10.39±1.10
▼ Electroporation	0.26±0.07
▽ Combination	8.79±2.21

Cumulative amount (μg/cm^2)

Time (h)