

Supplemental Information

Table SI. Comparative Summary of Nanoemulgel-Based Transdermal Permeation Using Animal Skin Models

Type of loaded drug	Skin models	Formulation	Particle size (nm)	Permeation results	Conclusion	Ref
Glimepiride	Rat abdominal skin	Nanoemulgel + clove oil	141.9 ± 3.35 – 213.3 ± 2.55	J _{ss} = 70.06 ± 6.60 µg/cm ² .h K _p = 0.035 cm/h	The results showed that the nanoemulgel containing glimepiride with clove oil presented the highest permeation compared both the oral suspension and conventional gel formulations.	[12]
Diclofenac sodium	Rat abdominal skin	Nanoemulgel + cumin essential oil (F1, F2)	82.20 ± 5.82 (F2, 4% Cumin essential oil) 87.53 ± 3.34 (F1, 2% Cumin essential oil)	J _{ss} (µg/cm ² .h) F2 = 1.78 ± 0.03 F1 = 1.50 ± 0.06 Q at 24h (µg/cm ²) F2 = 34.75 ± 1.07 F1 = 28.39 ± 1.23	Nanoemulgel formulations containing cumin essential oil significantly enhanced the transdermal delivery of diclofenac sodium compared to conventional gel and marketed formulations	[13]
Clove essential oil	Rat abdominal skin	Nanoemulgel	81.53 ± 11.15	J _{ss} = 31.32 ± 0.40 µg/cm ² .h K _p = 13.44 ± 0.00 × 10 ⁻³ cm/h Q = 1786.61 ± 29.14 µg/cm ² ER = 16.76 ± 0.74	Clove essential oil nanoemulsion-based nanoemulgel exhibited the highest permeation compared to both nanoemulsion-based nanofibers and pure clove essential oil formulation.	[14]

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Chrysin	Rat abdominal skin	Nanoemulgel	156.9 ± 3.4	J _{ss} = 192.3 ± 10.9 mg/cm ² ·h K _p = 29.6 ± 2.3 /cm ² .min	Chrysin-loaded nanoemulgel significantly enhanced skin permeation and retention compared to conventional gel.	[15]
Ketoconazole	Rat skin	Nanoemulgel + clove oil, nanoemulgel + eucalyptus oil	Nanoemulgel + clove oil 67 ± 3.4 Nanoemulgel +eucalyptus oil 78 ± 5.2	Nanoemulgel+clove oil J _{ss} = 4.88 ± 0.01 μg/cm ² .h Q = 117 ± 7 μg/cm ² Nanoemulgel+eucalyptus oil J _{ss} = 4.55 ± 0.03 μg/cm ² .h Q = 108.34 ± 6 μg/cm ²	Nanoemulgel formulations (with clove and eucalyptus oil) significantly enhanced the skin permeation and retention of ketoconazole compared to conventional gel.	[16]
Fusidic Acid	Rat dorsal skin	Nanoemulgel + Myrrh oil	113.6 ± 3.21	J _{ss} = 111.2 ± 4.5 μg/cm ² .h ER = 3.10 ± 0.13	Fusidic acid containing myrrh oil-based nanoemulgel demonstrated the highest skin permeation efficiency, significantly outperforming both the conventional fusidic acid gel and the free drug suspension.	[17]
Dasatinib	Rat skin	Nanoemulgel	170.01 ± 30.26	J _{ss} = 2.11 ± 0.25 μg/cm ² .h	The nanoemulgel formulation significantly improved the skin permeation of dasatinib compared to the free drug gel.	[18]

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Leflunomide	Rat abdominal skin	Nanoemulgel	123.7	J _{ss} = 200.9 ± 12.3 µg/cm ² .h K _p = 33.48 ± 1.3 /cm ² .min x10 ⁻³	The Leflunomide nanoemulgel significantly enhances transdermal flux and skin retention compared to the conventional gel.	[19]
Selegiline	Rat abdominal skin	Nanoemulgel	183.4 ± 0.35	J _{ss} = 3.4632 ± 1.25 µg/cm ² .h K _p = 0.6926 ± 0.176 cm/h	Nanoemulsion gel significantly outperforms the conventional gel and alternative nanoemulsion formulations in terms of transdermal drug delivery efficiency.	[20]
Asiaticoside	Rat abdominal skin	Nanoemulgel	132 ± 5.84	Q = 5.05× higher than Asiaticoside Gel (nanoemulgel) Q = 13.65× higher than Asiaticoside Gel (nanoemulsion)	Nanoemulsion and Nanoemulgel significantly increased the permeability ratio of Asiaticoside by 13.65 times and 5.05 times, respectively, compared to regular Asiaticoside (P < 0.01, P < 0.01).	[21]
5-Fluorouracil	Porcine ear skin	Nanoemulgel, nanoemulgel + glycyrrhizin	64.1 ± 5.13	Nanoemulgel J _{ss} = 7.212 µg/cm ² .h K _p = 2.294 cm/h ER = 3.86× higher than 5-Fluorouracil Gel Nanoemulgel + glycyrrhizin	Glycyrrhizin-based 5-Fluorouracil nanoemulgel demonstrated the highest transdermal flux and enhancement ratio compared to nanoemulgel without enhancer and plain 5-fluorouracil gel	[22]

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				Jss = 9.109 $\mu\text{g}/\text{cm}^2\cdot\text{h}$ Kp = 2.898 cm/h ER = 4.87 \times higher than 5-Fluorouracil Gel		
Ketoconazole	Porcine ear skin	Poly- δ -decalactone based nanoemulgel	68.9 \pm 3.4	Jss = 1.819 $\mu\text{g}/\text{cm}^2\cdot\text{h}$ Kp = 0.047 \times 10 ⁻³ cm/h	The Poly- δ -decalactone based nanoemulgel showed significantly enhanced permeation for ketoconazole (5 \times higher flux) compared to the conventional gel formulation.	[23]
Propranolol HCl	Rat posterior skin	Nanoemulgel	14.57 \pm 0.25	Jss = 4.64 \pm 0.36 $\mu\text{g}/\text{cm}^2\cdot\text{min}$ Q = 583.38 \pm 15.07 $\mu\text{g}/\text{cm}^2$ ER = 2.65 \times more than gel formulation	Propranolol HCl nanoemulgel significantly enhanced permeation and skin retention compared to Propranolol HCl gel.	[24]
Oxaprozin	Rat skin	Nanoemulgel + Gaaultheria oil	196.2 \pm 5.1	Jss = 6.564 $\mu\text{g}/\text{cm}^2\cdot\text{h}$	Permeation result showed that nanoemulsion delivers faster, but nanoemulgel provides better retention and controlled delivery, making it a more balanced and practical choice for topical.	[25]
Miconazole	Rat skin	Nanoemulgel	170 \pm 3.1	% Ci = 29.67%	The nanoemulgel formulation provides a superior topical delivery system for miconazole nitrate, with enhanced skin permeation over conventional creams.	[26]
Andrographolide	Porcine ear skin	Nanoemulgel	203 nm	Q = 21.11 \pm 3.5 $\mu\text{g}/\text{cm}^2$	The formulas of andrographolide nanoemulgel penetrated into the stratum corneum layer, and	[27]

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					andrographolide was retained in the dermal and epidermal layers.	
Terbinafine HCl	Rat abdominal skin	Nanoemulgel (F1-F3)	F1 = 52.87 ± 10.52 F2 = 74.37 ± 3.45 F3 = 68.63 ± 0.93	F1 J _{ss} = 5.4631 μg/cm ² .h K _p = 1.0926 cm/h ER = 2.69 F2 J _{ss} = 5.4098 μg/cm ² .h K _p = 1.082 cm/h ER = 2.66×	All terbinafine-loaded nanoemulgels (F1–F3) showed significantly higher skin permeation compared to marketed emulgel. Among them, F3 exhibited the highest permeation rate (J _{ss}), lowest viscosity, smallest particle size, and no lag time, making it the most efficient and fast-acting formulation	[28]
Naproxen	Rat abdominal skin	Nanoemulgel + Gaultheria oil	209.2	J _{ss} = 17.447 μg/cm ² .h	The nanoemulsion formulation delivered the highest drug flux, showing the fastest permeation, ideal for rapid onset. the NEG AU formulation is superior overall due to its balance of permeability, sustained effect, safety, and patient compliance.	[29]
Methotrexate	Rabbit skin	Nanoemulgel + almond oil, nanoemulgel + olive oil, nanoemulgel + clove oil	28.58 ± 4.31 20.81 ± 2.87 17.52 ± 5.13	Nanoemulgel + almond oil J _{ss} = 2.124 μg/cm ² .h Q = 47.37 μg/cm ² Nanoemulgel + olive oil J _{ss} = 1.971 μg/cm ² .h Q = 43.21 μg/cm ²	Nanoemulgel, which used almond oil as a penetration enhancer, showed the highest flux and cumulative permeation of methotrexate. Nanoemulgel with olive oil and nanoemulgel with clove oil also showed improved permeation over methotrexate solution (control), but were less effective than nanoemulgel with almond oil.	[30]

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				Nanoemulgel + clove oil Jss = 2.016 µg/cm ² .h Q = 39.42 µg/cm ²		

Jss = steady-state flux; Kp = permeability coefficient; Q = cumulative amount permeated; ER = enhancement ratio of flux; %Ci = percent drug release relative to initial concentration.