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Nanotechnology-Enhanced Controlled-Release Systems in Topical Therapeutics

SUMMARY TABLE

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Table 1. Summary of Drugs Formulated in Nanoparticles and Showing a Controlled-Release Profile During Topical Delivery

	Type of loaded drug	Target treatment or effect	Challenges with conventional topical delivery	Types of nanoparticles formulated	Method of nanoparticle preparation	In vitro drug release pattern	Doses tested	Drug loading	In vitro/In vivo/Ex-vivo outcome	References
1	Miconazole	Fungal infection	Poor skin penetration	PNCs and LNCs	Nano precipitation	LNCs showed more sustained release than PNCs	5 mg	24%	PNCs showed a better zone of inhibition (19 mm) than LNC (11 mm)	[18]
2	Terbutaline sulfate	Asthma	Low bioavailability of 15% and short half-lives	PNCs	Ionic gelation	Exhibited Higuchi diffusion model	3 mg	97%	1.33 times more ex-vivo permeation than the pure drug-hydrogels	[19]
3	Ondansetron	Motion sickness	Short half-lives	PNCs	Nano precipitation	Sustained release with Burst release	8 mg	78%	In vitro permeation (177 µg/cm^2.hr) than the aqueous solution(80 µg/cm^2.hr)	[20]
4	Retinol	Acne and psoriasis	Poor solubility and light sensitivity	PNCs	Solvent evaporation	Higuchi's model of diffusion	100–1000 mg	86%	High-efficiency encapsulation and protection from oxidation for at least eight week	[21]

5	Indomethacin	Inflammation	Poor solubility	NC and NS	Nano precipitation	Higuchi controlled-release model	300 mg	NC (98%) and NS (93%)	The NCs and NSs have 1.4 to 1.9 Fold percent edema inhibition beyond the normal gel in-vivo	[22]
6	Amphotericin B	Fungal infection	Toxicity and Poor solubility	PNCs	Nano precipitation	PH-dependent sustained release	1 mg/mL	85%	Improved its anti-leishmanial activity than the free Amp B	[23]
7	Benzocaine	Local anesthetic	Systemic adverse effects	PNCs	Emulsification/evaporation	sustained release	0.5%	96%	Good in vitro skin permeation (0.1 µg.cm^2) than the emulsion (0.04 µg.cm^2)	[24]
8	Deferoxamine	Diabetic ulcer	Low absorption of less than 15%	SLNPs	Cold homogenization	Sustained release profile	1 mg/mL	60%	Lacks in-vivo and ex-vivo data	[28]
9	Minoxidil and finasteride	Alopecia	Absence of scientifically approved treatment	LNPs	Ultrasonication	Sustained release for minoxidil, not for finasteride	No data	finasteride (70%) and minoxidil (30%)	Low in vitro skin penetration of the drugs	[29]
10	Vitamin A	Inflammation	Irritation at high concentration	SLNPs	High-pressure homogenization	Sustained release	0.5%	100%	No data available	[30]
11	Domperidone	Motion sickness	Poor bioavailability lower than 15%	LNPs and nanostructured lipid carriers	Hot homogenization and ultrasonication	Exhibited controlled release	10 mg	90%	Promising delivery systems for poorly water-soluble drugs,	[31]
12	Aceclofenac and Capsaicin	Pain and inflammation	Poor percutaneous permeation	Nanoemulgel	Solvent evaporation	Sustained release Manner with first-order	aceclofenac (750 mg) and capsaicin (5 mg)	No data	2.02 & 1.97-fold more permeation of Aceclofenac and capsaicin. suggesting the potential of this combination therapy to treat psoriasis	[35]

13	Etodolac	Rheumatoid arthritis	Poor aqueous solubility	Nanoemulsion	High shear homogenization and ultrasonication	Sustained release following non-fiction drug transport	1 to 5%	92%	50% paw edema inhibition in vivo	[36]
14	Piroxicam	Pain and inflammation	Low aqueous solubility	Nanoemulgel	High-pressure homogenization	Sustained release pattern	0.4%	79%	The analgesic activity was 1.66 times higher than the commercial gel	[37]
15	Ciprofloxacin	Bacterial keratitis	Precipitation upon ocular application	Nanoemulsion	Hot homogenization and ultrasonication	Controlled release with initial rapid	0.1-0.3% W/v	98%	2.1-fold transcorneal permeation than ophthalmic solution	[38]
16	Posaconazole	Fungal infection	Low oral bioavailability	nanoemulgel	Classic titration method	Zero-order Higuchi matrix kinetics	0.1%	96%	Better antifungal activity in comparison to the pure drug gel	[40]
17	Eprinomectin	Parasite treatment	High hydrophobic nature	Nanoemulgel	Homogenization/ultrasonication	Zero-order kinetics	0.33g	No data	The permeability of the nanoemulgel via the skin was 8 fold than the suspension,	[41]
18	Oxybutynin	Hyperhidrosis	Systemic side effects	Nanoemulgel	Emulsification	Sustained release pattern	0.1%	100%	12% of skin permeations as compared with no detectable permeation with the pure drug	[42]
19	Dapsone	Dermatologic conditions	Poor physicochemical properties	Liposomes	Ethanol infusion	Sustained release	0.1 mg	73%	No data available	[46]
20	5-fluorouracil and tretinoin	Skin warts		Liposomes	Ethanol injection method	Zero-order and Higuchi kinetics	1 mg/ml	Fluorouracil (72 %) and tretinoin (69 %)	Gradual release of drugs & safety as tested by histological evaluation	[47]
21	Hesperidin	Wound healing	Poor topical availability	Lipid-polymer hybrid nanoparticles	Emulsion solvent evaporation	Sustained release pattern	0.25%	93%	Potent in vitro antioxidant activity but lacks in-vivo data	[52]

22	Norfloxacin	Topical infection	Frequency of application and poor patient compliance	Lipid-polymer hybrid nanoparticles	Emulsification solvent evaporation	Controlled drug release	200 mg	73%	Good antibacterial activity against *Pseudomonas aeruginosa Staphylococcus aureus*	[53]
23	Hydrocortisone	Topical inflammation	Low skin permeability	Lipid-polymer hybrid nanoparticles	Single-step nanoprecipitation	Sustained release for a long time	0.5%	85%	Excellent anti-inflammatory activity in the croton oil-induced rosacea model	[54]
24	Oleanolic acid (plant extract)	Inflammation	Low permeability	Cubic liquid crystal nanoparticles	Homogenization and ultrasonication	Non fikcian diffusion	6–10%	68%	A more sustained anti-inflammatory effect than the marketed mometasone (std)	[58]
25	Acyclovir	Ocular fungal infection	Short ocular contact time and poor ocular permeation	Cubic liquid nanoparticles (cubosomes)		The release followed Higuchi's kinetics	0.1%	1 mg/g (loading)	Adhere on the ocular surface and to resist the lacrimation on porcine cornea and no toxicity of the formulation	[59]
26	Curcumin	Wound healing and infection	Poor solubility and rapid degradation	Silane-hydrogel nanoparticle	Sol-gel based polymerization	Controlled and sustained release manner	1%	10 µg/mg	Inhibited in vitro growth of (MRSA) and Pseudomonas Aeruginosa and enhanced wound healing	[62]
27	Mometasone	Chronic rhino sinusitis	Highly lipophilic and poor aqueous solubility	Mesoporous nanoparticles	Sol-gel method	Sustained release pattern	100 mg	41%	Increased permeation and delivery of mometasone than the commercial nasal spray	[64]
28	Erianin	Psoriasis	Poor water solubility	Dendritic mesoporous silica nanoparticles	Biphasic stratification approach	Sustained release pattern	30 nM	53%	Enhanced anti-proliferative effects on HaCaT cells and improved localized delivery in porcine skin	[65]
29	Fluconazole	Fungal infection	Low solubility and dermal absorption	Pristone carbon nanotubes	Ultara sonication and centrifugation	92% released after 8 hrs	50 mg	89%	No data available	[70]
30	Quercetin	Cancer (as an antioxidant)	Limited solubility and stability	Chitosan carbon nanotubes	Ultrasonication	Sustained release (ph-dependent release)	100µg/mL	38%	Significant Hella cancer cell death and the cell viability	[71]

									Decreased to 44% higher Compared to pure quercetin (57%)	
31	Aspirin	Diabetic retinopathy (anti-pain and anti-inflammatory)	Poor bioavailability by the ocular route	Albumin nanoparticles	Coacervation	Sustain release with 90% released over 72 hrs	0.4%	81%	No data available	[74]
32	siRNA (anti-Rela siRNA)	Atopic dermatitis	Poor topical bioavailability	Oligopeptide nanocarrier	Solid phase method	No data available	No data	No data	Reduced TNF-α and IL-6 levels in mice	[75]
33	Umbelliferone	Pain and inflammation	Limited water solubility	Carbopol nanocomposites	Green hydrothermal reaction	Sustain release (95 % released over 24 hrs)	10 mg	96%	27% edema reduction in-vivo	[77]

LNC = lipid nanocapsules; NC = nanocapsules; NS = nanospheres; PNC = polymeric nanocapsules; SNLP = solid-lipid nanoparticles.