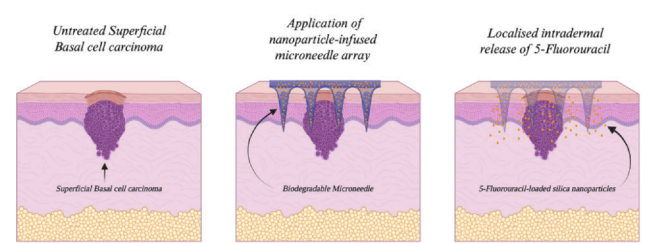


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Transdermal Delivery of 5-Fluorouracil via Nanoparticle-Infused Microneedles: A Pre-Clinical Study in Superficial Basal Cell Carcinoma

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Background: Topical 5-fluorouracil (5-FU) is an established treatment for superficial basal cell carcinoma (SBCC), but limited penetration into the dermis may reduce therapeutic effectiveness. Microneedle-based transdermal delivery systems offer a minimally invasive approach to enhance local drug deposition. This pre-clinical study evaluates biodegradable microneedle arrays incorporating 5-FU-loaded silica nanoparticles as a targeted delivery platform for SBCC.



Schematic of transdermal delivery of 5-fluorouracil via nanoparticle-infused biodegradable microneedles for superficial basal cell carcinoma. (A) Untreated lesion. (B) Microneedle application bypassing the stratum corneum. (C) Localised intradermal drug release.

Methods: Silica nanoparticles were synthesised and loaded with 5-FU at increasing initial drug masses (0.28-1.39 mg; 1-5 w/w%). Nanoparticle size, polydispersity, surface charge, loading efficiency, and encapsulation efficiency were characterised using dynamic light scattering and zeta potential analysis. Optimised formulations were incorporated into biodegradable carboxymethylcellulose-based microneedle matrices fabricated under controlled vacuum conditions. Microneedle morphology, nanoparticle distribution, degradation behaviour, and drug release profiles were assessed under simulated physiological conditions over 72 hours.

Results: 5-FU-loaded silica nanoparticles demonstrated stable nanoscale dimensions (109.7-195.8 nm) with low polydispersity (0.08-0.17) across all formulations. All particles exhibited negative zeta potentials (-25.17 to -46.70 mV), indicating good colloidal stability. Increasing initial drug mass improved loading efficiency up to 3 w/w% (0.84 mg), which achieved the highest loading efficiency (8.58%) and encapsulation efficiency (4.54%). Further increases in drug input resulted in reduced encapsulation efficiency without proportional loading gains. The selected formulation was successfully incorporated into microneedle arrays with uniform needle formation and sustained drug release over 72 hours.

w/w %	Initial mass (mg)	Size by DLS (nm)	Zeta-Potential (mV)	PdI	Loading Efficiency (%)	Encapsulation Efficiency (%)
1	0.28	174.5	-26.03	0.1688	2.13	3.94
2	0.56	162.1	-46.70	0.1540	4.03	4.38
3	0.84	190.8	-25.17	0.1118	8.58	4.54
4	1.11	195.8	-27.28	0.0837	7.05	2.85
5	1.39	109.7	-34.57	0.1685	5.15	2.23

Characterisation of 5-fluorouracil-doped silica nanoparticles showing the relationship between initial drug mass, particle size, surface charge, dispersity, and drug loading efficiency.
Conclusions: Biodegradable microneedles incorporating 5-FU-loaded silica nanoparticles provide a feasible transdermal delivery system for superficial basal cell carcinoma. The platform demonstrates controlled drug loading, stability, and sustained release, supporting further ex vivo and in vivo evaluation for non-invasive SBCC treatment.

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