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## Formulation and evaluation of fluconazole loaded nanosponges for improved topical drug delivery

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### SUMMARY

Fluconazole (an antifungal drug) loaded nanosponges (NS) were prepared by an emulsion solvent diffusion method using ethyl cellulose as the polymer. Prepared formulations were evaluated for various physicochemical parameters and in-vitro drug release. NS of fluconazole were discrete, free flowing nanosized particles with perforated orange peel-like morphology as shown by SEM analysis. A topical hydrogel formulation based on the drug loaded NS showed a prolonged release profile for the drug. Kinetic modelling on release data showed that the best fitted model was Higuchi model and release mechanism was by Fickian diffusion. FTIR and PXRD results confirmed the absence of any drug polymer interaction and stability of drug in the delivery system.

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### INTRODUCTION

Conventional topical systems such as ointments and creams are less effective due to their poor efficiency as delivery vehicles and are associated with side effects due to uncontrolled release of drug from the formulation. Therefore, attention is shifted towards development of particulate carrier systems such as microspheres, liposomes and nanoparticulate carriers for controlled delivery of drugs to specific skin regions (Ghanbarzadeh and Arami, 2013). In recent years more focus has been drawn towards the nanoparticulate systems e.g. nanosponges (NS), as they offer more precise control of the release of drug (Jain et al., 2014). NS are class of polymer based colloidal structures having nanosized cavities. A wide variety of topical agents can be safely incorporated into NS for getting benefits of these systems (Sharma and Pathak, 2011). Local anaesthetics, antifungals and anti-acne are among the potential categories of drugs that may be easily formulated as topical NS based

formulations.

The current study aimed to prepare and evaluate a hydrogel formulation based on fluconazole (an antifungal agent) loaded NS. Formulations were evaluated for pharmacotechnical properties and in-vitro release studies.

### MATERIALS AND METHODS

Fluconazole (FZ) was received as gift sample from Mass Pharma, Lahore, Pakistan. Ethyl cellulose, Polyvinyl Alcohol, Carbopol-940 and Propylene glycol were procured from Sigma Aldrich. All the other chemicals used were of analytical grade.

- 1) FZ nanosponges were prepared by emulsion solvent diffusion method as proposed by Sharma and Pathak, 2011. Six batches of nanosponges were prepared using different ratios of fluconazole (FZ) and ethylcellulose (EC) as shown in Table 1.
- 2) Prepared NS formulations were evaluated for particles size, entrapment efficiency, percentage yield and in vitro release of drug. Phosphate buffer solution (pH 5.5) was used as a dissolution

**Table 1.** Formulation and physical attributes of NS formulations

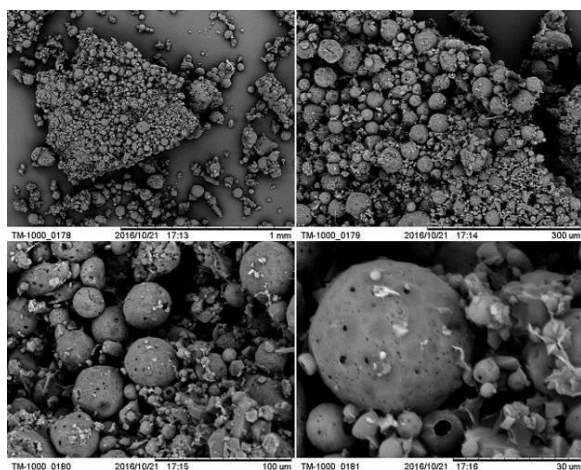
Formulation codes	FZ: EC ratio	% PVA used	Average particle size (nm)	Percent yield (%)	Entrapment Efficiency (%)
F1	1:0.3	0.5	220.19	92.43 ± 1.2%	79.32 ± 1.4%
F2	1:0.5	0.5	281.99	91.03 ± 1.0%	83.15 ± 2.3%
F3	1:0.7	0.5	358.67	89.14 ± 0.7%	82.30 ± 2.6%
F4	1:1	0.5	431.17	83.09 ± 0.9%	84.06 ± 1.5%
F5	1:1.3	0.5	512.38	87.21 ± 1.6%	86.11 ± 0.6%
F6	1:1.5	0.5	624.06	79.54 ± 0.2%	89.02 ± 0.8%

medium. Structural analysis was performed by SEM, PXRD and FTIR spectroscopy techniques.

- 3) Nanosponge based hydrogel was formulated by using carbopol 940 as a polymer.

## RESULTS AND DISCUSSION

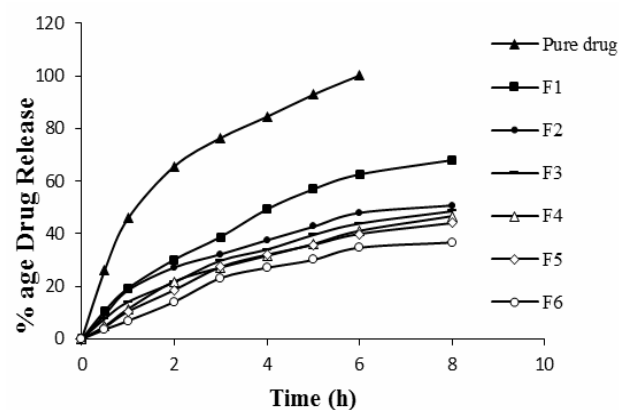
Table 1 shows particle size and physical attributes of NS formulations prepared by varying concentration of polymer ethyl cellulose. The prepared formulations showed nanosized particles in the range of 220-725nm. The mean particle size was considerably affected by drug: polymer ratio. The relatively smaller particle size is due to lower concentration of polymer providing lesser time for droplet formation. Formulation F3 shows comparatively better values of parameters of percent yield, entrapment efficiency and average particle size. SEM analysis (Figure 1) of this formulation showed spherical shape spongy structures having orange peel like appearance.



**Fig. 1.** SEM picture of F3.

The in-vitro release profiles of the formulated FZ nanosponges and pure fluconazole are illustrated in Figure 2. General trend shows decrease in the release of drug from nanosponges with the increase in polymer contents. Theoretically, this slower drug

release is ascribed to increased path length for drug diffusion. The pure drug dissolved almost completely at the end of 6 h due to solubility in phosphate buffer of pH 5.5. Among all formulations, F1 released higher amount of drug (68.03%) at the end of 8h which is due to small particle size (220.19 nm) providing large surface area for drug release (Higuchi). FTIR and PXRD results confirmed the absence of any drug polymer interaction and stability of drug in the delivery system. Hydrogel preparation based on FZ loaded NS showed acceptable formulation parameters.



**Fig. 2** Comparison of release profile of NS formulations.

## CONCLUSIONS

A nanosponge based topical hydrogel formulation of an antifungal drug, fluconazole was successfully prepared by emulsion diffusion techniques. These formulations showed better sustained release of drug over extended period of time.

## REFERENCES

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