Improved Antifungal Activity of Itraconazole Using Multiple Combination of Bioadhesive-Thermosensitive In Situ Vaginal Gel-Gel Flakes-Solid Dispersion in Candidiasis Rat Model

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BACKGROUND

The treatment of vaginal candidiasis using conventional dosage form resulted in ineffective therapy.

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As one of antifungal agents, the effectiveness of itraconazole (ITZ) is hampered by its poor aqueous solubility.

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Mucoadhesive-thermosensitive in situ vaginal gel containing gel flake- solid dispersion of ITZ could overcome the problems

OBJECTIVES

Develop mucoadhesive-thermosensitive in situ vaginal gel containing gel flake- solid dispersion of ITZ to improve antifungal activity in vaginal candidiasis in rat model.

METHODS

Table 1. The composition of gel flakes loaded with SD-ITZ formulations (% w/v)

Formula	SD-ITZ gel flakes (equal to pure ITZ)	PF-127	PF-68	BKC	HPMC	HEC
F1	1	20.00	-	0.01	-	-
F2	1	17.50	2.50	0.01	-	-
F3	1	15.00	5.00	0.01	-	-
F4	1	12.50	7.50	0.01	-	-
F5	1	10.00	10.00	0.01	-	-
F6	1	15.00	5.00	0.01	0.20	-
F7	1	15.00	5.00	0.01	0.40	-
F8	1	15.00	5.00	0.01	0.60	-
F9	1	15.00	5.00	0.01	-	0.20
F10	1	15.00	5.00	0.01	-	0.40
F11	1	15.00	5.00	0.01	-	0.60

Solid dispersion optimization and preparation

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Gel flakes optimization and preparation

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Gel flakes optimization and preparation

RESULTS

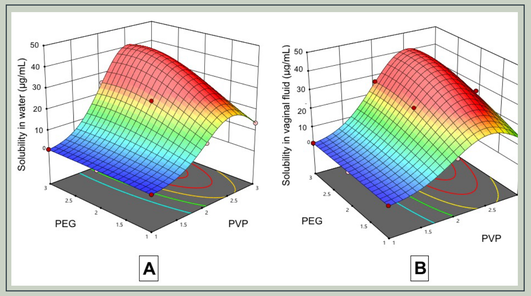

Figure 1. Representative UV-Spectra of CAB-MeOH, blank thermosensitive and mucoadhesive gel, (A); CAB-SVF and blank vaginal tissue (B)

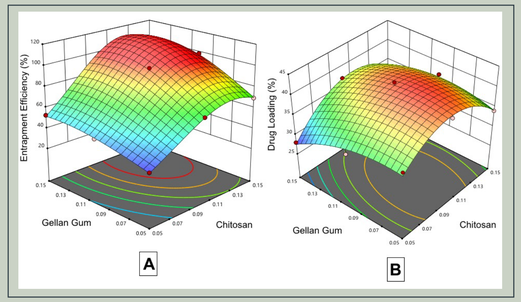

Figure 3. Optimization process describing the representative response surface plots showing the effect of the selected factors on (A) EE and (B) DL of the optimized formulations

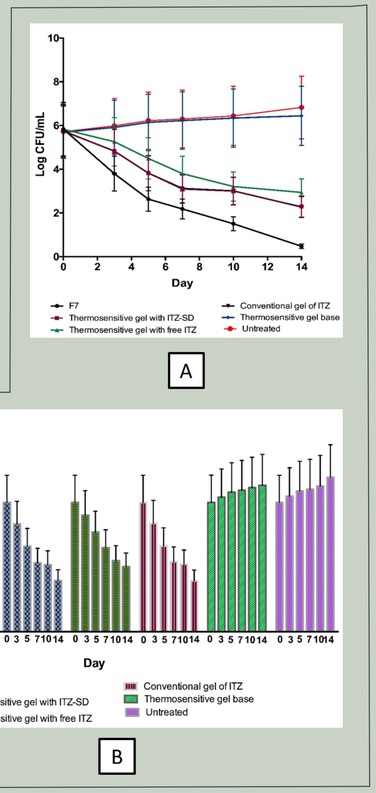

Figure 5. The results of in vivo antifungal activity studies expressed in (A) log CFU/mL and (mean ± S.D., n=3) (B) percentage of C. albicans population remaining (mean + S.D., n=3). The incorporation of the solid dispersion technique and gel-flake system in the formulation of the bioadhesive-thermosensitive in situ vaginal gel led to the most significant decrease of the growth of Candida albicans reaching <1 log colony-forming units (CFU)/mL, indicating the improvement of ITZ antifungal activity compared to other treated groups.

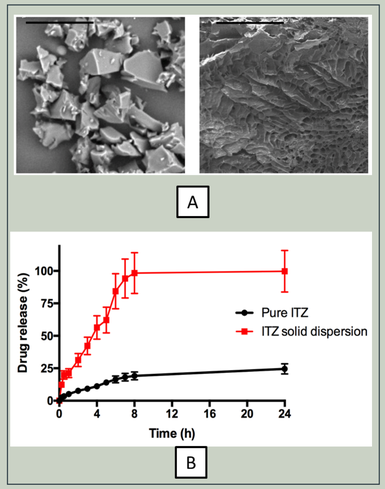

Figure 2. (A) The morphologies of free ITZ (left) and SD-ITZ (right) observed under SEM with the scale representing 50 mm. (B) The drug release profiles of pure ITZ (black line) and SD-ITZ (red line) (mean ± S.D., n=3). It was found that the formulation of ITZ into solid dispersion could enhance the solubility of ITZ.

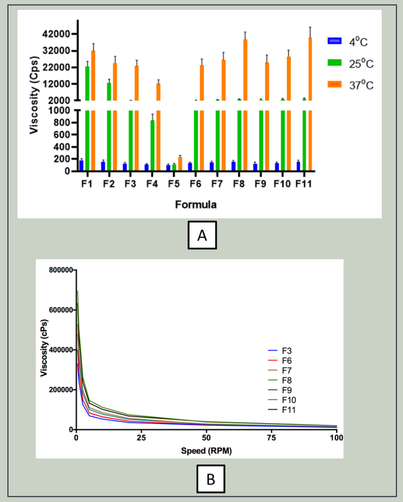

Figure 4. Figure 7. The results of (A) measured viscosity at 4°C, 25°C, and 37°C (mean ± S.D., n=3) and (B) the rheology behavior of bioadhesive-thermosensitive in situ vaginal gel.

CONCLUSIONS

The incorporation of ITZ into bioadhesive-thermosensitive in situ vaginal gel and gel flakes-solid dispersions could significantly enhance the solubility of ITZ and improve in vivo antifungal activity in candidiasis rat model.

REFRENCES

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