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Ketoconazole coated silver nanoparticles-A point antidandruff agent

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SUMMARY

The antidandruff activity of ketoconazole coated silver nanoparticles (AgNp) of 4±2 nm towards the dandruff scales collected from human volunteers by disc diffusion method was investigated. The minimal inhibitory concentration (MIC) of ketoconazole and ketoconazole coated AgNp during incubation with the dandruff causing fungi- *Malassezia furfur* was also studied. Antidandruff activity was highest with ketoconazole coated AgNp when compared to ketoconazole and AgNp individually. MIC was 0.06 mg/ml for ketoconazole, 0.026 for AgNp and 0.0135 mg/ml for ketoconazole coated AgNp. Results revealed the synergistic antidandruff activity of ketoconazole and AgNp. It was concluded that AgNp enhanced the activity of ketoconazole. This is because Ketoconazole acts on fungi at the level of cell wall, while AgNp powerfully penetrates through the membrane leading to complete eradication of the fungi.

Key words : Silver, Nanoparticles, Dandruff, Ketoconazole.

Dandruff is one of the serious problem in the society, characterized by scaling of scalp and skin. Persistence of dandruff may lead to itching and hair loss (Al-waili, 2001). *Malassezia* species is well recognized as a causative organism for dandruff (Squire and Goode, 2002). *Malassezia furfur, Malassezia* sympodialis, *Malassezia sloofia, Malassezia pachydermatis, Malassezia globusa* and *Malassezia restructa* are some examples for dandruff causing fungi (Gupta *et al.*, 2000). Association between *Malassezia furfur* and dandruff in human beings is well recognized (Samuel *et al.*, 2005). Antidandruff shampoos are formulated with azoles like ketoconazole, fluoconazole, and itracocnazole (Odds *et al.*, 2004). Ketoconazole was reported to be effective in the treatment of subjects with severe dandruff (Pierard-Franchimont *et al.*, 2002). In spite of several commercially available ketoconazole based antidandruff shampoo, dandruff recurrence is more frequent. Further, resistance of dandruff to antifungal agent is also of immense interest due to the development of resistant strains. Hence, development of a novel and efficient dandruff agent to prevent recurrence is essential.

Nanotechnology is a rapidly growing science of producing and utilizing nanosized particles that measure in nanometer (1nm= 1 billionth of a meter). Inorganic nanoparticles possess low toxicity and versatile properties like wide availability, rich functionality, good biocompatibility and potential capability of target delivery, driving forces for delivery and controlled release of target drugs (Kim, 2006). Silver in minute concentration is highly toxic to germs with low MIC values, while relatively non toxic to human cells. Microbes are unlikely to develop resistant against silver as they do against conventional and highly targeted antibiotics (Chen *et al.*, 2005, Ping and Zang *et al.*, 2006).

Drug nanoparticle hybrid system have widely been found useful in the enhancement of bioavailability, bioactivity and stability of drugs used in various infections. Drugs like sulphonamide, sulphadiazine and sulphamerazine complexed with silver showed enhanced activities against *Aspergillus* and *Candida* species (Wright *et al.*, 1999). Nanosilver has fastest and broadest spectrum fungicidal activity which makes it a good candidate to eradicate fungal infection without recurrence (Wright *et al.*, 1999). Silver is also reported to enhance the generation of reactive oxygen species which in turn degrade the cell membrane. Silver catalyze the denaturation of disulphide bridge in the cellular protein, thus denaturing the tertiary structure and function of cellular proteins (Fig. 1).

CH_2-S-S-CH_2

(Tertiary structure of functional protein with disulphide bridge)

↓ 2(H)

CH_2-SH + HS-CH_2 (Denatured protein)

Fig. 1 : Denaturation of protein by silver induced reduction

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