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FLUCONAZOLE LOADED SOLID LIPID NANOPARTICLES AS POTENTIAL CARRIER FOR BUCCAL DRUG DELIVERY FOR ORAL CANDIDIASIS TREATMENT

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ABSTRACT

The aim of present work was to develop and evaluate Fluconazole loaded solid lipid nanoparticles (SLNs) based gel for buccal drug delivery for the treatment of Oral candidiasis. Fluconazole (FZ) is an azole antifungal agent having broad spectrum activity against dermatophytes, moulds, yeasts, fungi. Fluconazole loaded SLNs systems were developed by Solvent injection method using Glycerol monostearate (GMS) as a solid lipid and Tween 80 as a surfactant. Developed SLNs were evaluated for particle shape and size, polydispersity index (PI), entrapment efficiency (EE) and drug release profiles. Process and formulation parameters were optimized. The FZ-SLNs based gel was prepared using Carbopol 934 as a gelling agent. The SLNs based gels were evaluated for physical appearance, pH determination, spread-ability, drug content and stability studies, in vitro drug release. Transmission electron microscopy confirmed that FZ-loaded SLNs were spherical. The particle size of the FZ-loaded SLNs was in the nano range of 203±5.5 nm which is suitable for drug penetration through buccal mucosa. The polydispersity index (PDI) showed a relatively narrow size distribution and was found to be in the range of 0.154- 0.201 and Zeta potential was found to be negatively charged which was -21.6. The entrapment efficiency was found to be84.3%. Thus, the study concludes that SLNs based gel of FZ gives a sustained release profile of FZ and has the potential for promising drug delivery carrier for local and systemic treatment of Oral candidiasis through the buccal mucosa

Key Words: Oral candidiasis, Fluconazole, Solid lipid nanoparticles, antifungal, sustained release.

INTRODUCTION

Fungal infections are becoming more common at an alarming rate, which poses a significant challenge to medical experts. It has become more common in wealthy nations over the past few decades and has been rising. It has a significant socioeconomic impact, high rates of morbidity and mortality, and affects over one billion people annually (Kainz *et al.,* 2020).

Oral candidiasis is a significant oral dermatological condition because it iscaused by the overgrowth of candida species in the oral mucosa, which can be brought on by both systemic and local causes. Oral candidiasis is an opportunistic infection of the oral cavity caused by an overgrowth of yeast like fungus called Candida. Oral candidiasis is the most common human fungal infection especially in early and later life.

The important Candida fungus is *C. albicans, C. tropicalis, C. glabrata, C. pseudotropicalis, C. guillierimondii, C. krusei, C. lusitaniae, C. parapsilosis* and Cstellatoidea. Among all these, .*C albicans* is the commonest one. *Candida albicans* is responsible for 40-60% of candidiasis cases. *C. albicans, C. glabrata* and *C. tropicalis* represent more than 80% of isolates from clinical infection (Wille *et al.,* 2013).

C. albicans is a common oral commensal that often doesn't create any issues for healthy individuals. More than 17 types of candida can infect deep tissues and the oral mucosa. Even though *Candida albicans* is still the most common cause of candidiasis, there has been a rise in the number of non-albicans Candida (NAC) species that are isolated from oral lesions and the bloodstream **(**Akpan and Morgan, 2002).

Numerous systemic and local predisposing conditions cause commensal candida to turn into pathogenic candida. Dentures, corticosteroid inhalers, and xerostomia are examples of local factors; immunosuppressed states, such as HIV/AIDS, leukaemia, malnutrition, age-related decreased immunity, endocrine dysfunction, systemic chemotherapy, radiation therapy, and the use of systemic corticosteroids, immunomodulatory drugs, xerogenic drugs, and broad-spectrum antibiotics, are examples of systemic factors. Recently psoriasis has been described as a predisposing factor for OC (Ghannoum and Radwan, 1990).

Therefore, antifungal medications are advised to reduce the frequency and severity of Candida infections; azoles group is the first group to be indicated for treating oral candidiasis. Fluconazole (FLZ) is a synthetic triazole derivative of the third generation and a broad-spectrum antifungal agent used for skin fungal infections as well as serious systemic fungal infections. Because fluconazole inhibits cytochrome P450, it prevents lanosterol from converting to ergosterol by rupturing the fungal cell membranes (Rencber *et al.,* 2019).

Depending on the severity and course of the illness, FZ is administered orally or locally as the first line of treatment for oral candidiasis. When FZ is used orally, severe side effects include rash, diarrhoea, upset stomach, and hepatotoxicity are frequently observed. For simple oral candidiasis, local treatment of FZ is advised as the initial option since systemic medication side effects can be prevented (Abu-Elteen and Abu-Alteen, 1998).

Drug delivery via the buccal mucosa provides a number of benefits, including avoiding first-pass metabolism, a high blood supply, and drug breakdown in the gastrointestinal (GI) tract. It can be used for local or systemic treatment. The non-keratinized portions of the human buccal mucosa absorb substances more quickly than the keratinized epithelium and skin combined. Nevertheless, a significant drawback that results in low bioavailability and efficacy is the low drug delivery penetration via the buccal mucosa. It is recommended to use drug delivery with nanoparticles to address this issue.

Nanoparticulate carrier technology such as solid lipid nanoparticles (SLNs) have gained attention in many fields of pharmaceutics. The first generation of lipid nanoparticles, or SLNs, are made of solid lipids and can be used to encapsulate medications or active

substances in a lipid matrix. Sub-micron colloidal particles, or SLNs, have a diameter of 50–1000 nm and are made of physiological lipids that have been dissolved in water or an aqueous surfactant solution. Solid lipid nanoparticles are appealing due to their potential to improve therapeutic performance because of their special qualities, which include small size, large surface area, high drug loading, and phase interaction at the interface (Kittiwisut and Kraisit, 2020).

The use of biodegradable lipids in SLNs provides several benefits over conventional carriers or other systems, including reduced toxicity and biocompatibility, drug protection from hazardous environments, avoiding organic solvents, controlled drug release, increased permeability and bioavailability, and large-scale production. A noteworthy benefit is the excellent efficacy of these carriers for encapsulating medications that are poorly soluble in water, as FZ. Furthermore, the medicine enclosed in the SLNs penetrates the skin more readily due to their small size.

So, the aim of this study was to formulate and characterize Fluconazole loaded solid lipid nanoparticles. The lipid nanoparticles were incorporated in gel for convenient delivery through buccal cavity.

MATERIALS AND METHODS

Materials

Fluconazole, Glycerol monostearate, Compritol 888ATO, Precirol ATO5, Carbopol 934was gifted by Micro labs Ltd (R&D) Kudlu, Bangalore. Tween80, ethanol, phosphate buffer 7.4 and distilled water all used were of analytical grade and used as received.

Methods

Screening of lipids

One of the most important steps in determining a lipid's capacity to fully solubilize a drug is screening its constituents. This process entails choosing the right lipid to load the maximum amount of drug.

For this purpose, we used three lipids which are (Glycerol monostearate, Compritol 888ATO, Precirol ATO5) to evaluate the solubility of fluconazole in terms of mass. The proportions of each solid lipid to Fluconazole (95:5mg) were physically mixed in test tubes and then heated to 70°C for 30 min using a water bath. The solubility of fluconazole in the melted lipids was visually analysed to ascertain if the lipids would be able to dissolve the fluconazole completely, depending on the presence or absence of the drug crystals (Vaghasiya *et al.,* 2013). For further production, fluconazole-loaded SLNs were prepared using the lipid that totally dissolves the drug or dissolves it better than the other lipids.

Preparation of Fluconazole loaded SLNs

For the preparation of Fluconazole loaded Solid Lipid Nanoparticles, Solvent Injection Method was used (Butani *et al.,* 2016).

(a) Preparation lipid phase – Mix the optimized quantity of drug with the selected lipid in 10 ml of ethanol. Melt the lipids in magnetic stirrer for 10 min. at 60-70°C. Then the lipid phase was obtained.

(b) Preparation of aqueous phase – Add optimized quantity of Tween 80 in 50 ml of water and stir.

Lipid phase drop was added into aqueous phase dropwise with needle at 70°C temperature was maintained. Pre emulsion was formed after 30 min. Then sonicate the SLN for 2-5 min. Cover the container with aluminium foil.

Preparation Fluconazole loaded SLNs Gel

Incorporate the Fluconazole entrapped SLN into gel. Prepare the gel by adding optimized quantity of Carbopol-934 in 40 ml of water. By using homogenizer, homogenized and mix the gel for about 45 min. Solid lipid Nanoparticles pre-emulsion is incorporated into prepared gel and stirred it for another 10 min (Souto and Muller, 2006).

Optimization of different variables for Fluconazole loaded SLN

Various formulation variables, i.e. lipid conc. (0.15,0.25,0.4,0.5,0.6gm), drug conc.(25mg, 50mg, 75mg), temperature for melting of lipid (50-60°C,60-70°C, 65-75°C), surfactant tween 80 concentration (0.5ml, 1ml, 2ml), and Carbopol conc. (0.75gm, 1gm, 2gm) which could affect the properties of solid lipid nanoparticles were optimized to get small SLN with maximum drug entrapment. Various parameters were optimized by varying one parameter while keeping others constant and prepared nanoparticles were studied for their particle shape and size, polydispersity index, percentage drug entrapment.

Characterization of Fluconazole loaded SLNs

Particle shape of SLNs- The selected and prepared Fluconazole SLNs were characterized by Transmission Electron Microscopy (TEM) for its shape, using a copper grid coated with carbon film and phosphor-tungstic acid (1% w/w) as a negative stain. After being stained, samples were allowed to dry at room temperature for 10 minutes for investigation (Jenning *et al.,* 2000).

2.42 Particle size, PDI and Zeta potential- The average particle size (Z-AVERAGE SIZE) and polydispersity index (PDI) of prepared and selected fluconazole- SLNs were performed using zeta sizer at 25 under a fixed angle of 90 in disposable polystyrene cuvettes. 1 ml sample was taken from each formulated nano-dispersion and dispersed with 10 ml of double distilled water. The samples were ultrasonicated for 5 min. prior to size determination to measure the primary particle size. Then the sample was taken in disposable sizing cuvette and placed in the instrument for particle size and zeta potential measurement (Ahmed *et al.,* 2014).

Determination of Entrapment Efficiency - The entrapment efficiency of all prepared fluconazole SLN was observed by centrifugation of Solid lipid Nanoparticles for 20 min with 3000 rpm. The supernatant is separated which contain the un- entrapped drug and measured by UV spectroscopy in 260λ. The amount of Drug unentrapped in SLN is determined by this equation:

$$\% \text{ Entrapment efficiency} = \frac{(\text{Winitial drug} - \text{W free drug}) * 100}{(\text{W initial drug})}$$

Where, w initial drug is the mass of initial drug used in assay and W free drug is the mass of free drug detected in supernatant after centrifuge of dispersion (Kumara *et al.,* 2007).

Characterization of Fluconazole SLNs Topical Gel

Physical examination of SLN Gel - Selected gel formulae were inspected visually for their homogeneity, colour, consistency (Lim and Kim, 2002).

Determination of pH- 1 gm of fluconazole-SLN gel was dispersed in 100 ml of water then pH was measured by using pH meter.

Spreading-ability- 1 gm of gel was placed within a circle of 1 cm diameter pre-marked on the glass plate over which a second plate was placed. Then a weight of 500 gm was allowed to rest on the upper plate for 5 min. the increase in the diameter due to spreading of gel was noted (Li *et al.,* 2006).

Stability studies- Sometimes during the storage of lipid nanoparticles, problems such as particle agglomeration and drug leaking from nanoparticles are observed. To ensure that the prepared SLNs were stable, a stability study on the optimized formulation was performed to measure any change in the particle size, PDI, entrapment efficiency and zeta potential on the storage of the formulation. The formulation was kept undisturbed at room temperature for 30 days. The purpose of doing stability studies was to observe the safety, efficacy and stability in any temperature and storage condition. The particle size, PDI, zeta potential and entrapment efficiency of formulation were measured just after formulation and after 30 days of storage (Lippacher *et al.,* 2001).

Determination of Drug Content- For determining the drug content, 1 gm of formulated fluconazole loaded SLN gel was dissolved in 100 ml of phosphate buffer 7.4 pH using volumetric flask. Solution was filtered and the yield was estimated spectrophotometrically at 260 nm.

In-vitro **drug release studies**- The SLN formulation were evaluated by using cellophane membrane. 1gm of fluconazole loaded SLN gel was filled in the membrane which was tied with thread in burette stand and emerged in the phosphate buffer of pH7.4 kept in the container which is on the magnetic stirrer. Magnetic stirrer was allowed to stir at the temperature up to 37°C. A specific volume of media was withdrawn at specific time intervals at 1, 2, 3, 4, 5, 6, 7 hour and equal volume of fresh dissolution media was added and maintain the sink condition. By using UV spectroscopy at 260nm calculate the drug release (Liu *et al.,* 2007).

RESULTS AND DISCUSSION

Screening of lipid

The screening of lipids was carried out to select a lipid with highest affinity for drug which will affect the entrapment. Three lipids were used in screening which were Glycerol monostearate, Compritol888ATO, Precirol ATO5 which was visually analysed.

Preparation of Fluconazole loaded SLNs

Solvent injection method was the method of choice for Solid Lipid Nanoparticle preparation for drugs showing high solubility lipids. Method works on the principle of diffusion of solvent from lipid phase to aqueous phase leading to lipid precipitation.

Glycerol monostearate (0.5 gm) and Drug (fluconazole) (50 mg) were dissolved in 10 ml of ethanol, maintained at an elevated temperature of 60-70°C and melt the lipid on magnetic stirrer for 10 min. Then this solution was injected into an aqueous solution [Tween

80(1ml) and Water (50ml)] maintained at similar temperature (60-70°C) and formed lipid suspension. Then suspension was sonicated, Solid Lipid Nanoparticles was prepared. Then these SLN incorporate into gel using Carbopol- 934(1 gm) as gelling agent. It is a very simple, easy method with fast production rate and no involvement of sophisticated instrument.

Optimization of different variables

The different variables involved in the preparation of SLN were optimized, including lipid conc., drug/lipid ratio, temperature for melting of lipid, surfactant concentrationand Carbopol conc. to obtain nanosized particles with maximum drug entrapment efficiency.

(a). Lipid employed in the production of SLNs was first subjected to optimize by varying the concentration of lipid from 0.15g, 0.25g, 0.4g, 0.5g and 0.6g, keeping another parameter as constant. Prepared formulation was further characterized on the basis of Particle size, PDI, Zeta potential. Optimized formulation L4 with **0.5 g** was selected as it showed optimum size of **201±3.07nm**, PDI of **0.186** and zeta potential (mv) of **-21.4**. Hence, **L4** was selected for further optimization. The observations are recorded in table no. 1 and graph of it is recorded in figure no. 1.

(b). Another parameter considered for optimization was Drug – lipid ratio on the basis of particle size and percent of drug entrapment efficiency. Three formulations with different drug concentration (25 mg, 50 mg, 75 mg) and constant lipid ratio were prepared refers to table no.1 and figure no. 2. It was concluded that on increasing the amount of drug, the entrapment efficiency increased up to drug: lipid ratio 50 mg: 500 mg while on further increasing drug concentration in the lipid, the entrapment efficiency gradually decreased (Table no.1). This could be due to the saturation of lipid with the drug. Same effect was observed on the particle size. So, **L4D2** was selectedfor further optimization processes whose particle size was **206±3.0** and entrapment efficiency was **83%**.

(c) Duration for melting of lipid in ethanol was 10 min. Lipid should get properly melted because it plays an important role in particle size and its entrapment efficiency. Optimization of temperature was recorded in table no.1 and figure no. 3 which showed that when temperature (50-60°C) was kept low, particle size and entrapment efficiency were also low as it doesn't get melted uniformly. When temperature (65-75°C) was kept higher, particle size and entrapment efficiency were less as compared to the temperature kept at **60-70°C** which show optimum particle size of **180 ±5.9** and entrapment efficiency of **86%**. So, **L4D2T2** was selected for further optimization process.

(d). The effect of surfactant was also observed on particle size and entrapment efficiency. Surfactant was added to stabilize to nanoparticles, reducing particle size, improving drug loading capacity and enhancing drug release properties. Aqueous phase was prepared with tween 80 in 50 ml of water. Three formulations were prepared with different concentration which was 0.5 ml, 1 ml, 2 ml in 50 ml of water. The particle size was found to be decreased upon increasing the concentration of tween 80. This might be because surfactant decreases the surface tension between organic phase and aqueous phase, which ultimately leads to the

formulation of nano range particles. However, on further increasing surfactant concentration, although the particle size decreases because of formation of micelles but the entrapment efficiency also decreases because of the leaching out of the drug. Therefore, at the concentration of 1 ml it shows optimum size of **189 ±8.5** with maximum drug entrapment which was **85%**. So, **L4D2T2S2** was selected for further optimization. The observation of optimization of surfactant refers in table no.1. and figure no. 4.

(e). The prepared SLN was incorporated in gel for which Carbopol-934 was used as gelling agent. The concentration of Carbopol-934 affects the viscosity of formulation, smoothness, spreading ability and drug content as well. L4D2T2S2 was final formulation of SLN which was incorporate into gel. Three formulation of gel was prepared with different concentration of gelling agent which was 0.75 gm, 1 gm, 2 gm. Higher concentration of Carbopol -934 causes thickening of gel and decreases the smoothness and on the other hand decreasing the amount of gelling agent, increases flowing ability of gel. The optimum consistency, semisolid, smooth and stable gel was obtained when **1gm was added in 40 ml of water** which shows drug content of **83%**. The observation of optimization was recorded in table no. 2 and figure no. 5. Hence, **L4D2T2S2C2** was the final optimized quantity for formulating Fluconazole loaded SLN gel.

Characterization of SLN and SLN incorporate gel

The plain SLN and SLN incorporate gel was characterized on the basis of particle shape, particle size and PDI, entrapment efficiency, physical examination of SLN gel, pH of SLN gel, spread-ability, stability studies, drug content, in-vitro release studies.

Shape of SLN particles -The shape of SLN particle and surface morphology of the particles was studied by Transmission Electron Microscopy (TEM). It was found from TEM images that the nanoparticles were almost spherical with smooth morphology, black dots represent the colloidal sizes of SLNs with no aggregation, well dispersed and separated on the surface. This indicates that the system made from solvent injection method was monodispersed. The images by TEM showed in figure 6.

Particle size and PDI OF Fluconazole loaded SLNs -The size of particle is considered one the most important factor because penetration mechanism through buccal mucosa greatly depends on it. Particle size was found to be **203±8.5** which is suitable for buccal delivery for the penetration of drug.PDI was found to be**0.186** which shows a homogeneous size distribution of the formulation. All formulations were negatively charged, the ZP was **-21.6 mv** indicating good stability of particles.

Entrapment efficiency -Prepared formula has an entrapment efficiency% was found to be **84.7%.** The results showed that increase in lipid concentration will increase the entrapment efficiency. High concentration of solid lipid leads to reduction of lipid crystallinity and increased imperfections in the crystal lattice of lipid which leaves enough space to accommodate drug molecules.

Physical examination of SLN gel - Fluconazole loaded Solid Lipid Nanoparticle was found to be white, viscous smooth, homogenous of semisolid consistency which was analysed visually.

pH determination of SLN gel- The pH of prepared fluconazole loaded SLN was found to be in range of 6.8 to 7.4 which resemble the pH of buccal mucosa.

Spreadability-Prepared SLN was found to be have great spreadable property.

Stability studies- The SLN formulation were kept at room temperature for 30 days to check the effect of storage on particle size, PDI, zeta potential and entrapment efficiency. The formulation was found to be the stable as it had the least change in the above parameters on storage.

***In-vitro* drug release studies**-The amount of fluconazole released from prepared SLN was determined by cellophane membrane using Phosphate buffer of pH 7.4 as dissolution medium. The results shows that gel contained fluconazole-SLNs were able to release fluconazole in controlled manner. The results are recorded in table no.8.

Table 1: Compositions of various SLNs formulations

Formulation code	Lipid conc.(gm)	Drug conc. (mg)	Temperature (°C)	Surfactant conc. (v/v)	Particle size (nm)	EE%	PDI	Zeta potential (mv)
L1	0.15	-	-	-	169 ±4.2	-	0.154	-12.7
L2	0.25	-	-	-	178 ±1.7	-	0.165	-14.9
L3	0.4	-	-	-	190±1.10	-	0.179	-18.5
L4	**0.5**	**-**	**-**	**-**	**201±3.07**	**-**	**0.186**	**-21.4**
L5	0.6	-	-	-	210±4.10	-	0.201	-23.7
L4D1	-	25mg	-	-	197 ±4.9	72%	-	-17.4
L4D2	**-**	**50mg**	**-**	**-**	**206 ±3.0**	**83%**	**-**	**-21.9**
L4D3	-	75mg	-	-	201 ±4.1	79%	-	-19.3
L4D2T1	-	-	40-50 °C	-	131 ±10	65%	-	-
L4D2T2	**-**	**-**	**60-70 °C**	**-**	**180±5.9**	**86%**	**-**	**-**
L4D2T3	-	-	65-75 °C	-	174 ±8.6	77%	-	-
L4D2T2S1	-	-	-	0.5 ml	210 ±12	69%	-	-
L4D2T2S2	-	-	-	**1 ml**	**189 ±8.5**	**85%**	-	-
L4D2T2S3	-	-	-	2 ml	140 ±10.7	76%	-	-

Table 2: SLNs formulation incorporate into Gel

Formulation code	Carbopol concentration (gm)	Viscosity of gel	Drug content
L4D2T2S2C1	0.75 gm	Semi-solid but unstable	78%
L4D2T2S2C2	**1 gm**	**Semi-solid and stable gel**	**83%**
L4D2T2S2C3	2 gm	Very thick	85%

Table 3: Screening of Lipids

S. No.	Lipids	Solubility
1.	Glycerol monostearate	Very soluble
2.	Compritol 888ATO	Sparingly soluble
3.	Precirol ATO5	Sparingly soluble

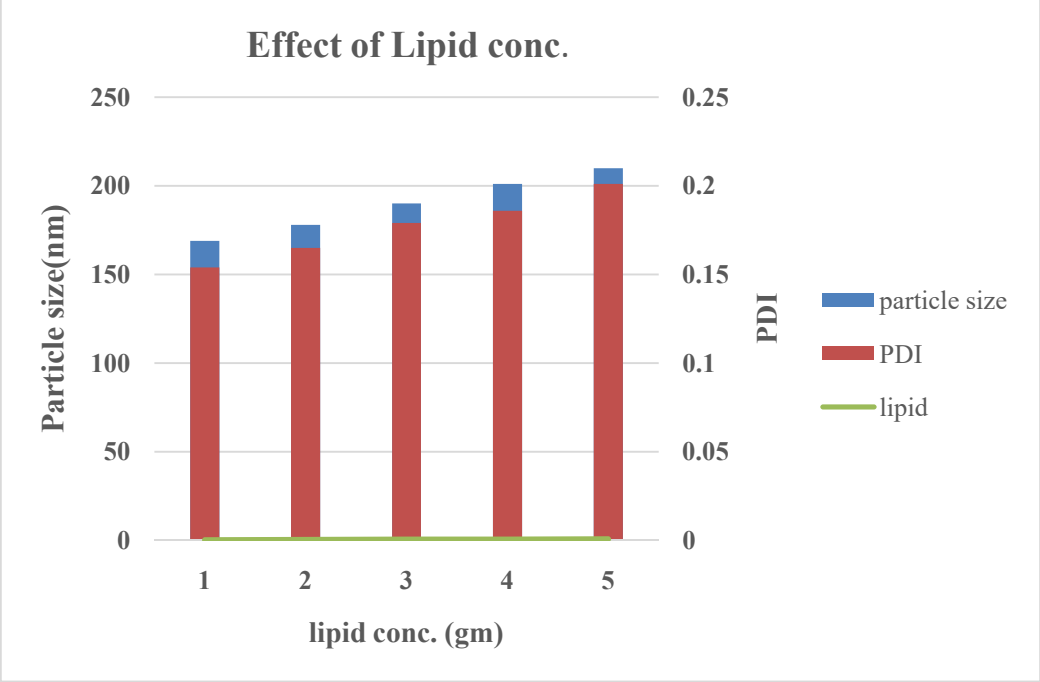


Figure 1: Optimization of lipid conc., graph is plotted between lipid conc. v/s particle size and PDI

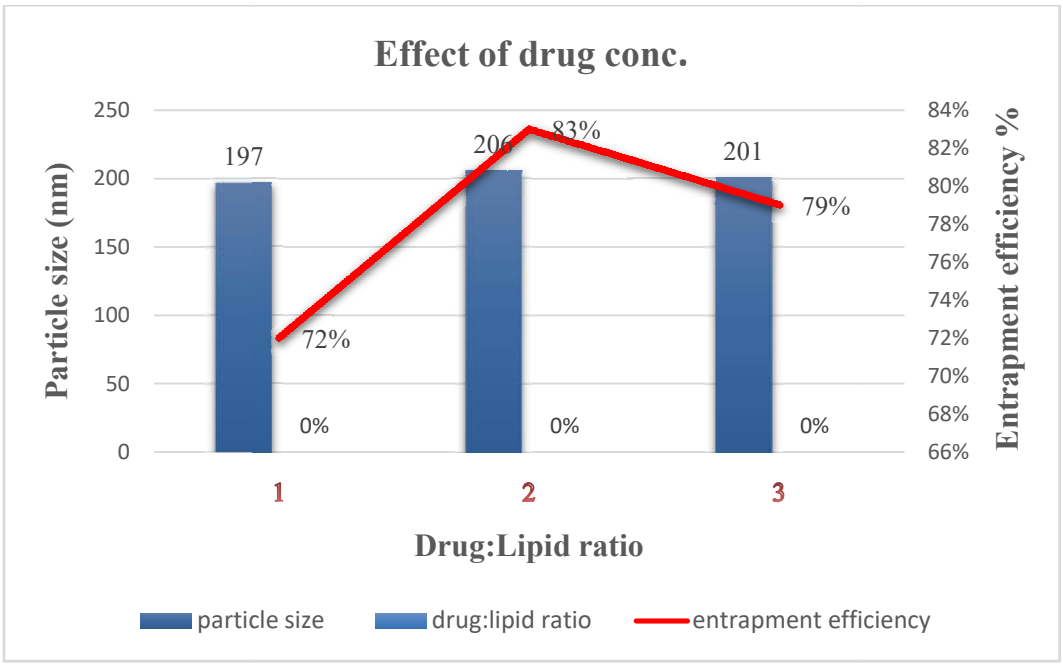


Figure 2: Optimization of weight of drug, graph plotted between weight of drug v/s particle size and entrapment efficiency

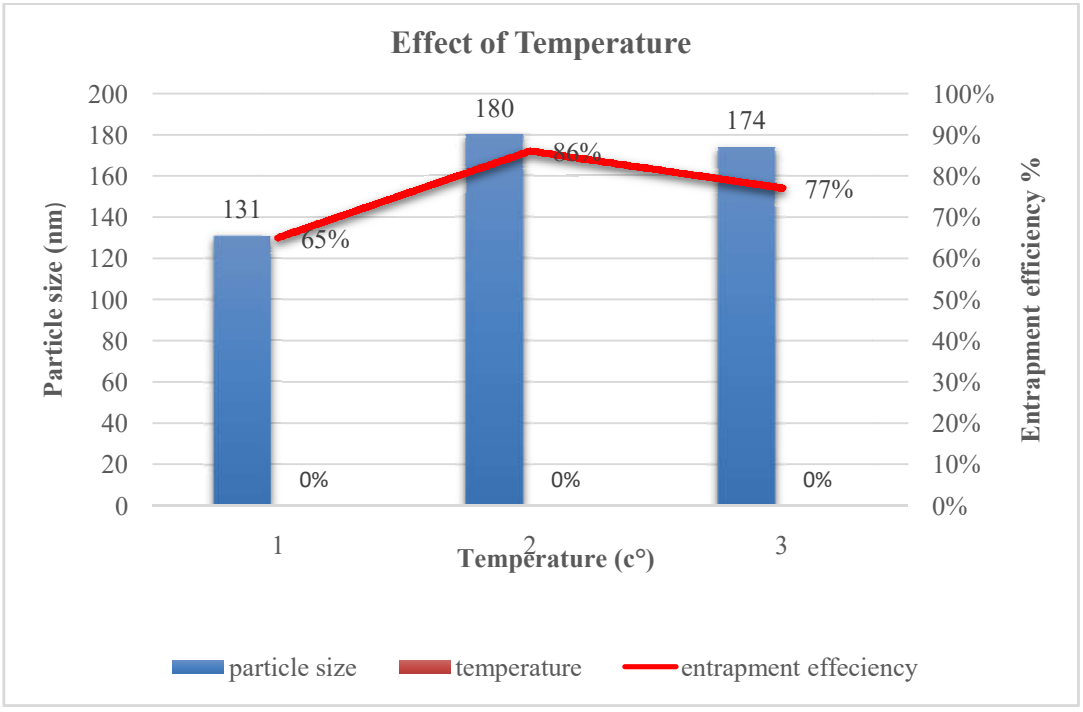


Figure 3: Optimization of temperature, graph is plotted between temperature v/s particle size and entrapment efficiency

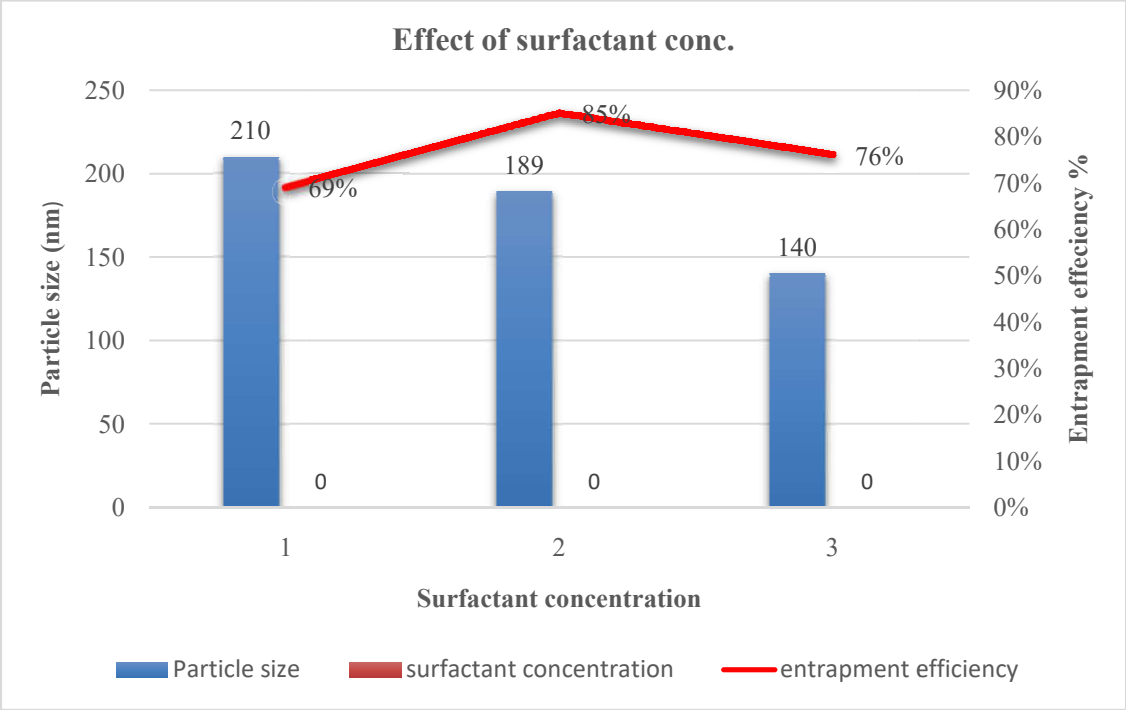


Figure 4: Optimization of surfactant conc., graph is plotted between surfactant conc. v/s particle size and entrapment efficiency

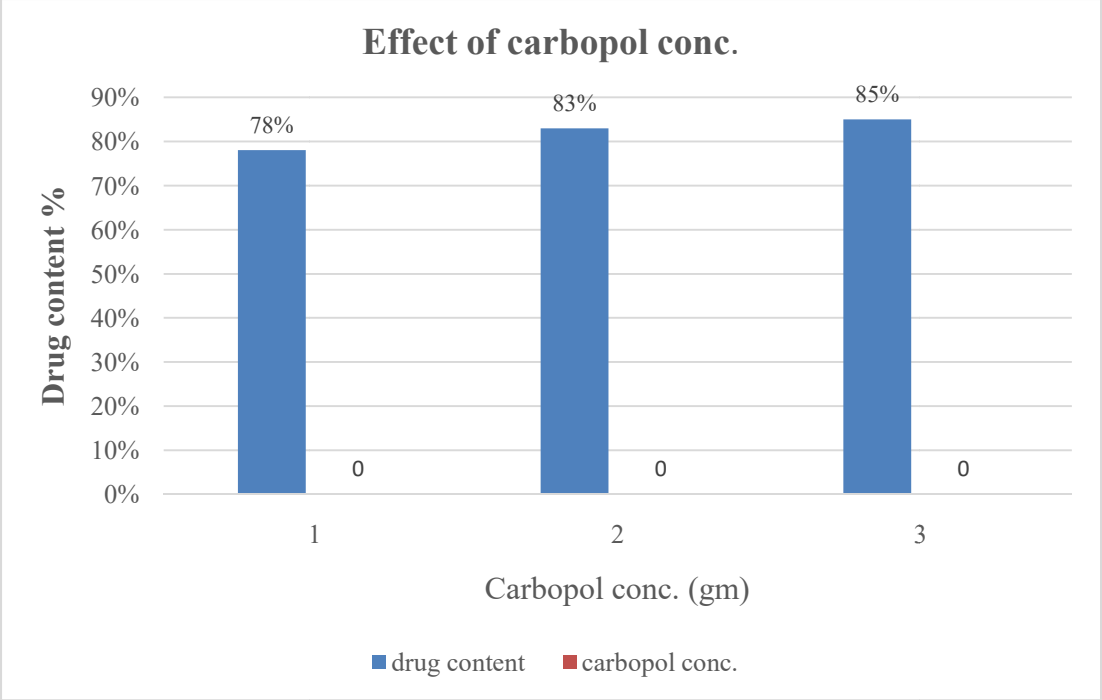


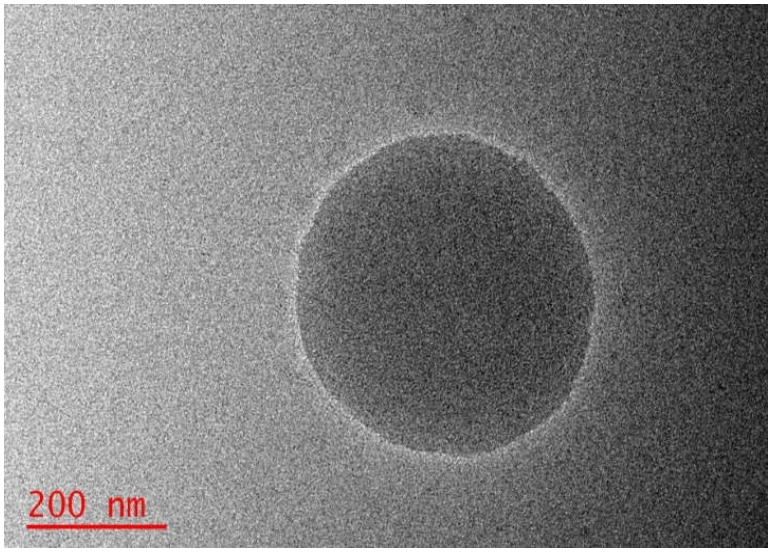
Figure 5: Optimization of Carbopol conc., graph is plotted between Carbopol conc. v/s drug content

Table 4: Optimized values for preparing SLN gel

Optimized parameter	Value	Parameter constant	Final code optimized
Lipid concentration	**0.5 gm**	Another parameter remains constant	**L4D2T2S2C2**
Weight of drug	**50 mg**	Another parameter remains constant	
Temperature	**60-70**°C	Another parameter remains constant	
Surfactant concentration	**1 ml**	Another parameter remains constant	
Carbopol-934 concentration	**1 gm**	Another parameter remains constant	

Table 5: Final Entrapment efficiency, particle size and Zeta potential

Formulation code	Particle size	Particle shape	Entrapment efficiency	Zeta potential (mv)
L4D2T2S2C2	203±8.5	Solid and spherical	84.7%	-21.6



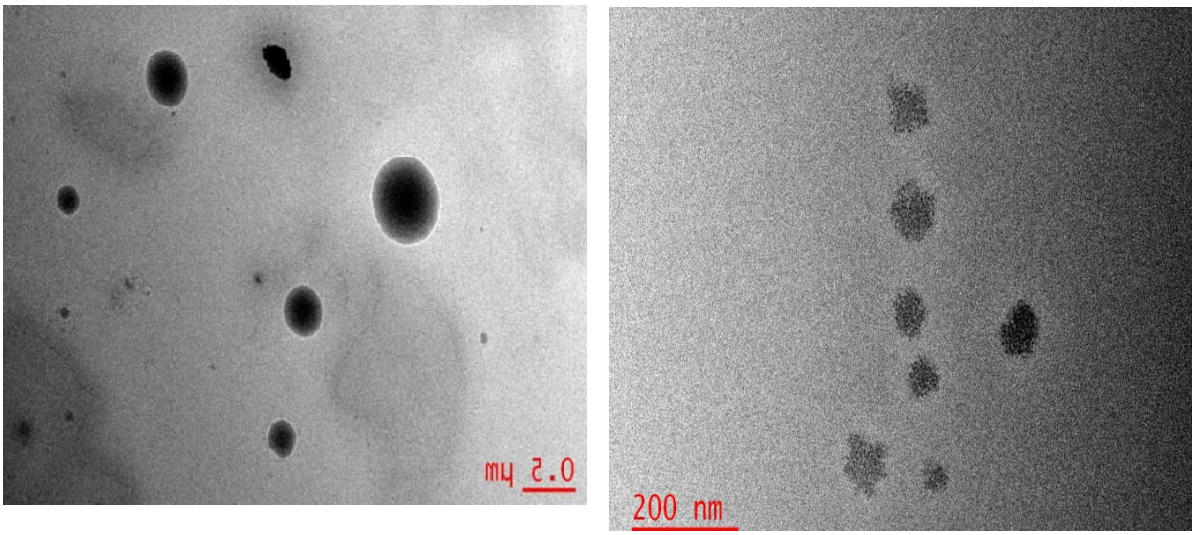


Figure 6: Images of SLNs particles by TEM

Figure 7: Fluconazole loaded SLNs Gel

Table 6: Characteristics of fluconazole-SLNs before storage

Formulation	Particle size	PDI	Zeta potential	Entrapment efficiency
SLN L4D2T2S2C2	203±8.5	0.186	-21.6	84.7%

Table 7: Characteristics of fluconazole-SLNs after 30 days storage

Formulation	Particle size	PDI	Zeta potential	Entrapment efficiency
SLN L4D2T2S2C2	207±8.8	0.189	-20.3	82.1%

Table 8: *In-vitro* drug release study

S. No.	Time	Drug release
1.	After 1 hour	4.17±0.7
2.	After 2 hours	21.75±1.6
3.	3 hours	40.31±2.9
4.	4 hours	63.45±3.10
5.	5 hours	76.49±5.1

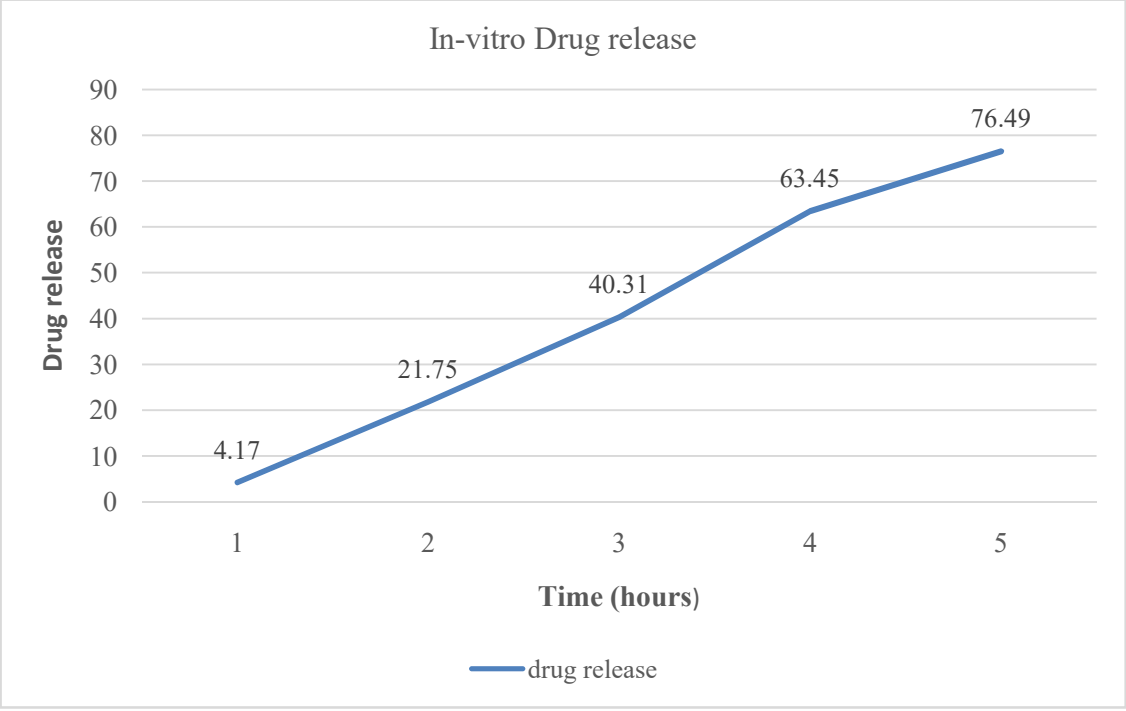


Figure 8: Graph of *in-vitro* drug release which is plotted between time and drug release

CONCLUSION

In the present work, fluconazole-SLNs were successfully prepared by Solvent injection method and successfully incorporated into Gel for buccal drug delivery. The results showed that the entrapment efficiency %, zeta potential, zeta size, morphology and the in-vitro drug release from fluconazole-SLNs dispersion and from fluconazole-SLNs gels were greatly affected by concentration of surfactant and concentration of the used lipid, conc. of drug, temperature and Carbopol conc. In-vitro drug release study indicate that Fluconazole loaded SLN bearing gel provides sustained release of Fluconazole. SLNs are in nano range which causes increase in surface area which entrap the drug in great extent and penetration through buccal cavity also depends on particle size. The study provides evidences that SLN could be a better module for prolonged release profile with wide applications in buccal cavity and will be safe and convenient for the patient.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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