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Original Research Article

Solid Lipid Nanoparticles based Hydrogel of Mycophenolate Mofetil for the treatment of Psoriasis

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Abstract: ***Background:*** Psoriasis is a type of chronic skin disease that has affected many people worldwide. Topical delivery in psoriatic skin has been addressed by the colloidal carrier system, such as Solid lipid nanoparticles. ***Objectives:*** The aim of this study was to develop and evaluate a solid lipid nanoparticle (SLN)-based topical gel containing mycophenolate mofetil for the effective treatment of psoriasis. ***Methods:*** Solid lipid nanoparticles (SLNs) have emerged as promising systems for topical drug delivery, aiming to enhance local bioavailability and improve drug penetration into the epidermis through close contact with the stratum corneum. In this study, SLNs were prepared using the solvent injection method with Precirol ATO5, Labrasol, and soya lecithin. The resulting formulations were characterized for particle size, size distribution, zeta potential, and morphology using transmission electron microscopy, and their performance was evaluated through in vitro and in vivo drug release studies. ***Results:*** Among the eight formulations developed, the one containing 0.2% Precirol ATO5, 0.03% soya lecithin, and 2% Labrasol showed the most promising results. This selection was based on key evaluation criteria, including particle size, zeta potential, polydispersity index, encapsulation efficiency, and overall drug content. To study the drug release behavior, in vitro release experiments were performed using a Franz diffusion cell with a dialysis membrane, with acetate buffer (pH 5.5) serving as the receptor medium. The release profile of the SLN-based gel (F8) was compared with a standard carbopol gel formulation. Results showed that the steady-state flux (Jss), a key permeability parameter, was significantly higher in the SLN-F8 gel, indicating improved skin permeation compared to the other tested formulations. ***Conclusion:*** In conclusion, the mycophenolate mofetil-loaded SLN-based hydrogel formulated with carbopol demonstrated strong potential for topical use, offering improved results compared to conventional oral administration

Keywords: Psoriasis, Solid lipid nanoparticles, Mycophenolate mofetil, Mycophenolic acid, Hydrogel

INTRODUCTION

Mycophenolate mofetil (MMF) is a modified version of mycophenolic acid (MPA), created to make the drug more effective and better tolerated. The original compound, MPA, was first identified in 1896 by Gasio, who extracted it from a fermentation process involving Penicillium stoloniferum. In recent years, medical studies have found that MPA can be beneficial in treating serious cases of psoriasis and rheumatoid arthritis [1-2]. Despite its potential, the use of MPA has been restricted because of side effects such as stomach irritation and blood-related issues. To overcome these problems, mycophenolate mofetil (MMF) was developed, providing improved absorption and fewer adverse effects than MPA [3]. As a result, MMF is now emerged as a promising option for treating chronic plaque psoriasis and

psoriatic arthritis. The first reported successful use of MMF in treating a severe psoriasis case appeared in 1997, showing marked improvement through a notable decrease in the Psoriasis Area and Severity Index (PASI) score [4]. Psoriasis is a chronic inflammatory skin disorder that can develop on different areas of the body, most often affecting the scalp, elbows, knees, and lower back. The condition's visible symptoms result from the accelerated production and abnormal maturation of skin cells, combined with inflammation and alterations in the skin's blood vessels [5].

Effective management of psoriasis often depends on using a platform used to administer drugs that can provide controlled, long-lasting delivery of medication, preferably targeting the affected skin directly [6]. A promising strategy for this is topical delivery through advanced colloidal carriers such as solid lipid nanoparticles (SLNs). These innovative systems are particularly beneficial for treating skin disorders like psoriasis because of their strong compatibility with the skin [7]. The components used in SLNs are generally safe for the skin's outer layer, the stratum corneum, and can gently modify its structure to enhance drug absorption without relying on extra chemical penetration enhancers.

To create a safer and more efficient topical delivery system for Mycophenolate Mofetil (MMF), it is essential to increase the concentration of drug at the target site and maintain its effect for a longer time, while reducing unwanted systemic side effects. SLNs provide a favorable approach, particularly for treating inflamed or damaged skin, since they are composed of non-toxic and non-irritating lipids [6]. Their tiny particle size enhances surface area, improves physical stability, and enables controlled, sustained drug release.

Due to close interaction of SLNs with the stratum corneum, they enhance the penetration of drugs into the skin. In addition, their occlusive nature helps minimize trans epidermal water loss, further facilitating the absorption of active compounds through the skin barrier. The topical application of SLNs also supports quicker market availability since it bypasses some regulatory hurdles linked with systemic delivery methods [8]. SLNs have already demonstrated potential as carriers for the sustained release of a variety of bioactive substances.

MATERIALS AND METHODS

2. Experimental section

2.1. Material and Methods

Mycophenolate mofetil was obtained from Panacea Biotech, Lalru, Punjab, India. Carbopol 940 was sourced from HiMedia Laboratories Pvt. Ltd., Compared with other delivery platforms like liposomes, SLNs are easier to manufacture on a large scale. Their lipid-based core structure makes them gentle and suitable for use on irritated or damaged skin [9]. The small particle size and large surface area of SLNs allow them to hold drugs more effectively, leading to better therapeutic outcomes. Some major advantages of SLNs include improved physical stability, protection of delicate drugs from breakdown, and the ability to control how quickly or slowly the drug is released. They also offer the potential for targeted drug delivery, enhancing overall treatment efficiency [10–11].

Unlike conventional topical formulations that may cause an initial burst release of the drug, SLNs offer a more controlled delivery, reducing the risk of systemic absorption and associated side effects [12]. This is especially relevant for MMF, which when taken orally, can cause several adverse effects such as gastrointestinal discomfort, leukopenia, and increased vulnerability to viral infections particularly diarrhoea in kidney transplant patients [13]. These issues are believed to stem from MMF's effect on rapidly dividing intestinal epithelial cells. Therefore, a topical delivery system could provide a safer and more localized treatment option, reduce systemic exposure while maintain therapeutic effectiveness at the target site [14-15].

SLNs are increasingly recognized as an efficient system for topical drug delivery, particularly for increasing local drug availability in the skin. By forming close contact with the stratum corneum, and also enhance drug penetration into the epidermis, allowing precise delivery to the affected area. The lipid materials used in SLNs are highly compatible with the skin and can gently modify its structure, improving drug absorption without the need for extra chemical enhancers [16]. Their tiny particle size enables better interaction with the skin surface, helping more of the drug reach deeper layers.

Building on these advantages, the present study aims to develop a hydrogel-based SLN formulation for delivering Mycophenolate Mofetil (MMF) topically to manage psoriasis. The SLNs will be systematically formulated, optimized, and incorporated into a gel to ensure easy application and good skin adherence. This delivery approach is intended to reduce MMF's systemic side effects while allowing controlled, sustained drug release ultimately enhancing treatment effectiveness and patient comfort.

Mumbai, India. Stearic acid, Precirol ATO 5, soya lecithin, and Labrasol were procured from Gattefosse, Mumbai, India. The dialysis membrane

used in this study was also purchased from HiMedia Laboratories Pvt. Ltd., Mumbai. The chemicals and solvents used were of AR grade quality to ensure the precision and reliability of the experimental

outcomes.

2.2 Screening of Components (Solubility studies)

To determine the saturation solubility of Mycophenolate Mofetil (MMF) in different surfactants, co-surfactants and several solid lipids were tested, including Compritol 888 ATO, Precirol ATO 5, stearic acid, glycerol monostearate, and a 1:1 blend of Compritol 888 ATO and Precirol ATO 5. Each lipid was heated to approximately 10°C above its melting point, after which 10 mg of the drug added to 500 mg of the molten lipid with continuous stirring. The process continued until the mixture became cloudy, indicating that the saturation point had been achieved [17].

To select an appropriate surfactant and co-surfactant, the solubility of MMF was tested in various surfactants, including Labrasol, Tween 80, soya lecithin, and Cremophor EL. An excess amount of drug was mixed with 5 ml of each surfactant in sealed vials, and then incubated in a shaking water bath at 37 ± 1°C for 72 hours to allow the system to reach equilibrium [18]. After this period, the mixtures were filtered through a 0.45 µm membrane filter. The clear filtrates were then diluted with methanol and analyzed using UV at 250 nm to measure the concentration of drug.

2.3 Preparation of Mycophenolate mofetil loaded SLN dispersion

SLNs containing MMF were formulated using the solvent injection method. In this process, accurately measured amounts of Precirol ATO 5 and soya lecithin were dissolved in a 1:1 mixture of acetone and ethanol under constant stirring with a magnetic stirrer at 70°C. Meanwhile, an aqueous solution of Labrasol were prepared by dissolving it in a suitable amount of water with continuous stirring. Once both phases were ready and maintained at the same temperature, the lipid solution was slowly introduced into the aqueous phase using a syringe, drop by drop, at a controlled rate of 5 mL/min with continuous stirring. The resulting dispersion was further mixed using a mechanical stirrer at 4000 rpm for one hour. To achieve a nanosized dispersion, probe sonication was applied afterward [19-20]. Multiple SLN formulations were developed by varying the concentrations of Precirol ATO 5 and Labrasol, as detailed in [Table 1]. These formulations were then used for subsequent evaluations.

Table no.1 Composition and of SLNs prepared by Solvent injection method:

S.No	Formulation code	Drug (%)	Precirol ATO 5 (mg)	Labrasol (%)	Soya lecithin (mg)	Acetone (ml)	Ethanol (ml)	Water (ml)	Total Vol (ml)
1	F1	0.1	100	0.5	30	5	5	50	50
2	F2	0.1	100	1	30	5	5	50	50
3	F3	0.1	100	1.5	30	5	5	50	50
4	F4	0.1	100	2	30	5	5	50	50
5	F5	0.1	200	0.5	30	5	5	50	50
6	F6	0.1	200	1	30	5	5	50	50
7	F7	0.1	200	1.5	30	5	5	50	50
8	F8	0.1	200	2	30	5	5	50	50

3.Characterization of Mycophenolate mofetil Loaded SLN Dispersion

The characterization of the SLNs included evaluating key parameters such as particle size and size distribution, zeta potential, and drug entrapment efficiency (EE).

3.1 Particle size and particle size distribution

The particle size of the solid lipid nanoparticle formulations was measured using a particle size analyzer. The polydispersity index (PDI) was also determined with a zetasizer, providing information on the uniformity of the particle size distribution and indicating the stability of the formulation [21].

3.2 Zeta Potential

The surface charge (zeta potential) of the MMF-loaded SLN droplets was measured using a Zetasizer 300 HAS [22].

3.3 Drug Entrapment efficiency

To evaluate the entrapment efficiency, 2 ml of the SLN formulation containing the drug was gently shaken to achieve a uniform dispersion. The sample was subsequently centrifuged in a refrigerated centrifuge at 15,000 rpm for 30 minutes. Following centrifugation, the supernatant was passed through a 0.2 µm Millipore membrane filter. The filtrate was then diluted with methanol, and the drug content was quantified using a spectrophotometer set to 250 nm. The entrapment efficiency (%) was finally determined using the standard formula (23):

Where, C_t = represent the concentration of total drug
C_r = represents the concentration of the unencapsulated (free) drug.

3.4 Drug content

The overall drug content of the prepared SLN formulations, encompassing both the incorporated and unentrapped drug, was assessed. Each sample was suitably diluted and examined using a spectrophotometer set at 250 nm to quantify the drug concentration. The total drug content was subsequently computed using the specified formula (24).

Drug Loading =Wt-W_f /Wn *100

$$\% \textit{Encapsulation efficiency} = Cr - Cr/Ct * 100$$

Where, W_f is amount of free drug, Wn is amount of total drug
Wn is weight of excipients used in formulation

4. In-vitro drug release studies of formulations

The in vitro release of the drug was evaluated using a Franz diffusion apparatus. This setup includes a donor chamber at the top and a receptor chamber below, with both parts enclosed within a water jacket to ensure constant temperature conditions. The diffusion unit has a capacity of 22.5 ml and provides an effective diffusion area of 2.303 cm². The receptor chamber was filled with acetate buffer (pH 5.5), and the temperature was maintained at 37 ± 1°C. Continuous stirring at 100 rpm was achieved using a Teflon-coated magnetic stir bar. A 1 ml portion of each formulation was placed onto the membrane in the donor compartment. At predetermined intervals over a 24-hour period, 2 ml aliquots were withdrawn from the receptor chamber through the sampling port and immediately replaced with fresh acetate buffer (pH 5.5) to maintain the original volume. The withdrawn samples were analyzed promptly for drug concentration using UV spectrophotometry at 250 nm, and the cumulative drug release was calculated over the study period.[25].

4.1 Transmission Electron Microscopy

The structure of the optimized formulation was observed with the help of transmission electron microscopy (TEM). One drop of sample was an excess solution by filter paper. One drop of phosphotungstic acid (1.0%) was stratified for staining. After applying phosphotungstic acid, any excess was gently wiped away with filter paper, and the sample was left to dry at room temperature for 30 minutes before observation. The grid was observed by TEM and by using imaging viewer software. The images were analyzed and captured (26).

5. Preparation of MMF loaded SLN based gel formulations

Carbopol 940 were selected as a gelling agent because of its good compatibility with SLNs and its ease of spreadability. Carbopol-based gels were prepared at different concentrations (0.5, 1, 1.5, and 2% w/w) by slowly dispersing the polymer in 50 mL of the optimized formulation with continuous stirring using a magnetic stirrer for about 1 hour. The dispersion was then gradually neutralized by adding triethanolamine drop by drop until a gel formed. After neutralization, the gel was left in the dark for 24 hours to allow complete swelling. For the plain gel, MMF was first dissolved in the required amount of methanol and then slowly incorporated into the Carbopol 940 solution that had been soaked overnight.

5.1 Characterization of MMF loaded SLN gel formulations

The formulations were evaluated visually and checked for spreadibility, odor, color, texture (like any grittiness), consistency, and pH level. (28).

5.2 In-vitro drug release study

The in vitro release of MMF from the suspension, carbopol gel, SLN dispersion, and SLN-based gel was examined using the dialysis bag technique, employing cellulose membranes positioned within a Franz diffusion cell. The receptor chamber was filled with acetate buffer (pH 5.5) and kept at 37 ± 1°C, while continuous agitation at 100 rpm was maintained using a Teflon-coated magnetic stir bar. In the donor chamber, 1 ml of the MMF-loaded suspension or SLN dispersion, and 1 g of the SLN-based gel containing 10 mg of MMF, were placed onto the membrane surface. At specified time intervals (2, 4, 6, 8, 10, 12, and 24 hours), 2 ml samples were withdrawn and immediately replaced with fresh acetate buffer to preserve the original volume. The collected aliquots were promptly analyzed for MMF content using UV spectrophotometry at 250 nm, and the cumulative release profile was subsequently determined.

5.3 Ex-vivo skin permeation studies

Ex vivo skin permeation studies were performed in a Franz diffusion cell equipped with rat abdominal skin. The receptor chamber was filled with acetate

buffer (pH 5.5) and maintained at 37 ± 1°C under constant stirring at 100 rpm using a magnetic stirrer. Three different formulations MMF suspension, MMF-loaded plain gel, and MMF-SLN-based gel each containing an equivalent amount of drug, were applied individually to the donor compartment. At specific time intervals, 2 ml samples were withdrawn from the receptor compartment and analysed spectrophotometrically at 250 nm. After each withdrawal, an equal volume of fresh acetate buffer was added to maintain a constant volume and ensure continuous contact between the skin and receptor medium. The experiment was carried out for 24 hours, and the cumulative amount of drug permeated through the skin was determined.

5.4 Release kinetics

To evaluate the mechanism of drug release from the delivery system, the ex-vivo permeation data obtained for the optimized SLNs and the SLN-incorporated hydrogel were fitted to various kinetic models, including zero-order, first-order, Higuchi, and Peppas–Korsmeyer models. Each model was subjected to regression analysis to identify which one most accurately described the release profile of the formulations.

RESULTS

6.1 Screening of components

Choosing the right solid lipid that can dissolve the drug the best is crucial for achieving the highest possible drug loading. The results of solubility of MMF in different solid lipids and surfactants are given in Figure 5.5 and 5.6. The maximum solubility of MMF was found in stearic acid (310±3.1mg/g) and Precirol ATO 5 (120±4.5mg/g). However, stearic acid was not selected for development of SLN based formulation because it was reported to reduce skin permeability of nano formulations and along with associated skin irritancy. Therefore, Precirol ATO5 was chosen as the lipid component to create solid lipid nanoparticles for delivering the drug topically.

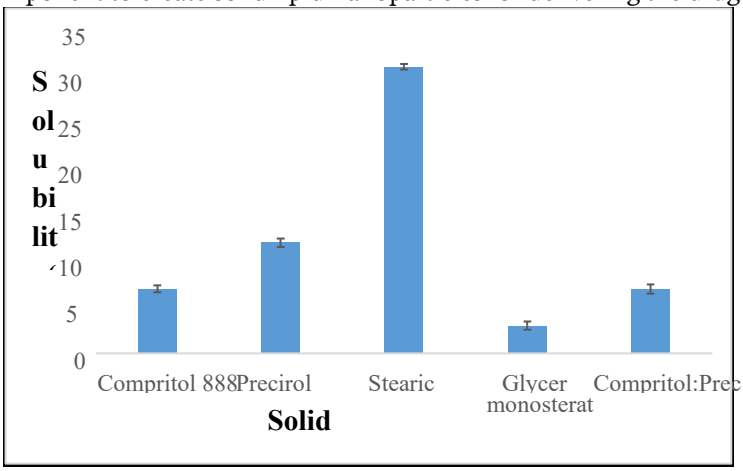

Figure 1. Solubility of MMF in various solid lipids

Among the surfactants tested, the highest drug solubility was observed with Labrasol (68.2 ± 3.19 mg/mL). Labrasol, a non-ionic surfactant, is widely used as a solubilizing agent and also helps enhance drug permeability. Based on these solubility studies, Precirol ATO 5 and Labrasol were identified as the most suitable components for the preparation of solid lipid nanoparticles.

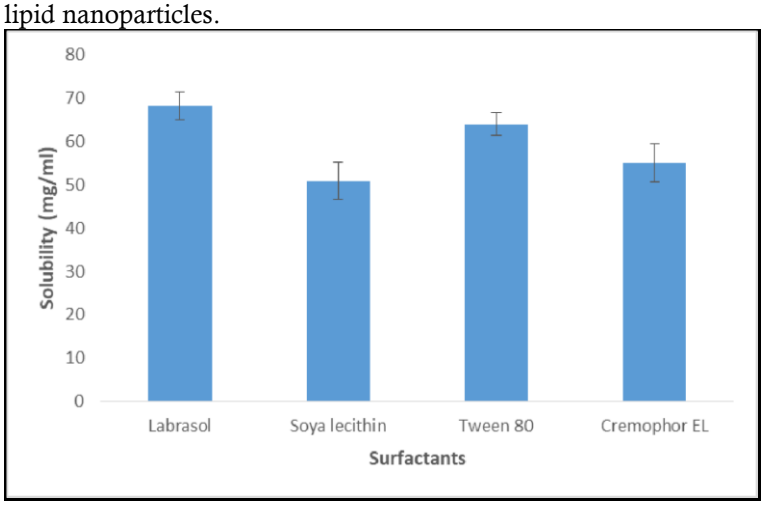

Figure.2 Composition and characterization of solid lipid nanoparticles (SLN):

6.2 Particle size:

Particle size determination is a major criterion for the preparation of dermal drug delivery systems that facilitate drug permeation through skin barrier. The particle size and PDI of the SLN formulations were measured using a particle size analyzer, and the results are presented in Table 3. The mean particle size across all batches ranged from 128 ± 0.004 to 194 ± 0.004 nm. The findings indicated that formulations containing higher lipid concentrations and lower amounts of surfactant produced larger particles. Conversely, increasing the surfactant level resulted in a reduction in particle size. These observations suggest that both lipid content and surfactant concentration significantly influence particle size, with higher lipid levels contributing to larger particles. Additionally, the polydispersity index (PDI) for all batches ranged from 0.303±0.004 to 0.256±0.001, indicating that the particles were evenly distributed and formed a uniform suspension in all the SLN batches.

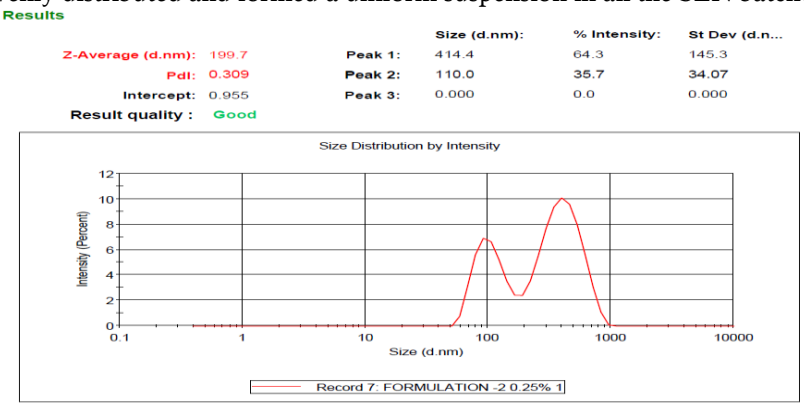

Figure 3 Graph representing the data of particle size and PDI of formulation F8

6.3 Entrapment Efficiency: The percentage of drug incorporated into the prepared SLNs ranged from 11.8±0.02% to 86.9±0.15%. For the chosen batch, the entrapment efficiency was 86.9±0.15%, and the drug loading was 0.401±0.001%. These results are detailed in Table 3. The high entrapment efficiency is likely due to the drug's lipophilic nature, which allows it to easily bind with the selected lipid matrix.

6.4 Zeta potential

The zeta potential of the drug-loaded SLNs ranged from –4.956 ± 0.020 mV to –13.73 ± 0.094 mV. The incorporation of MMF into SLN showed no influence on the zeta potentials of nanoparticles. A higher negative zeta potential creates a repelling force between the SLNs, which helps keep the nanoparticles from clumping together.

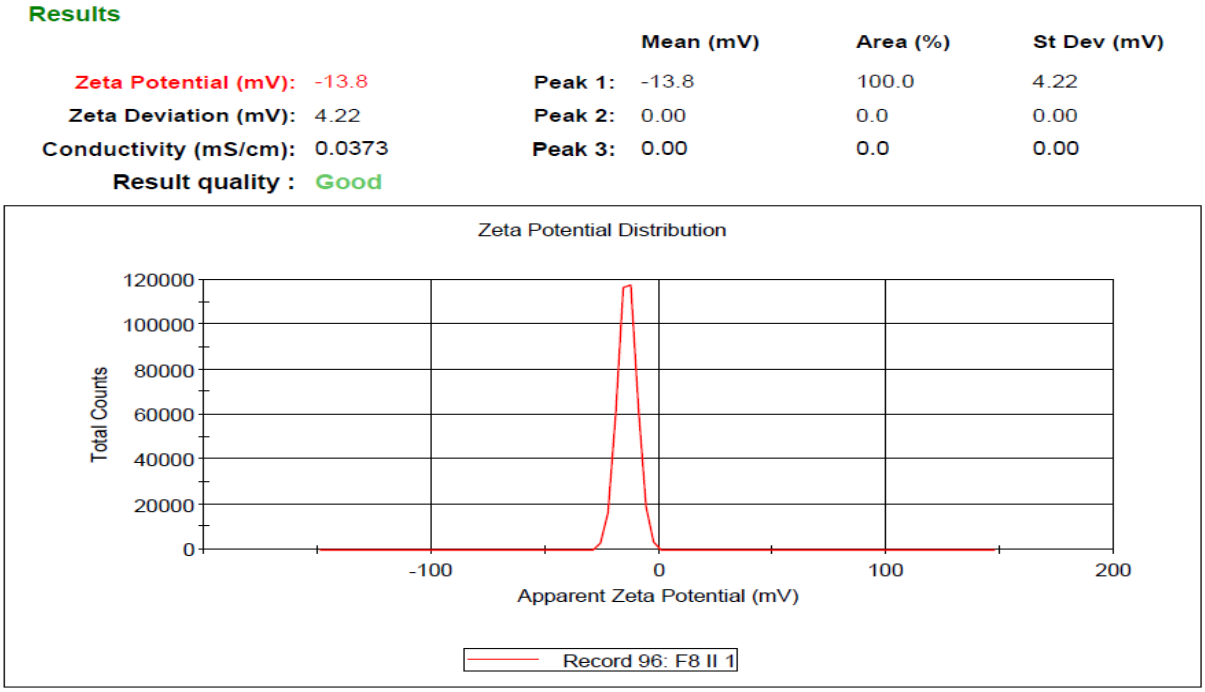

Figure. 4 Zeta potential of MMF loaded solid lipid nanoparticles of formulation F8

Table. no.3 Physicochemical characterization of prepared solid lipid nanoparticles formulations:

S.No	Formulation code	Particle size (nm)	Polydispersity index (PDI)	Zeta potential (mV)	Entrapment efficiency (%)	Drug loading (DL)
1	F1	135±0.004	0.303±0.004	-6.91±2.0	71±0.71	0.268±0.002
2	F2	128±0.002	0.319±0.003	-14±3.0	80.6±0.44	0.290±0.003
3	F3	142±0.004	0.310±0.002	-7.58±2.0	64.4±0.11	0.314±0.004
4	F4	157±0.005	0.308±0.002	-11.5±1.9	43.9±0.41	0.325±0.001
5	F5	168±0.002	0.291±0.002	-18.3±1.6	22.9±0.17	0.338±0.002
6	F6	186±0.003	0.279±0.004	-17.58±2.3	11.8±0.02	0.366±0.004
7	F7	192±0.003	0.577±0.003	-14.5±1.2	58.2±0.40	0.385±0.004
8	**F8**	**194±0.004**	**0.261±0.004**	**-22.1±3.2**	**86.9±0.15**	**0.401±0.001**

6.5 Transmission Electron Microscopy

The morphology of the selected MMF-SLN dispersion was examined using a transmission electron microscope, as illustrated in Figure 5.6. For the analysis, a drop of the dispersion was placed onto a carbon-coated copper grid and stained with 2% phosphotungstic acid. The sample was then left to dry for 10 minutes before being observed under the microscope.

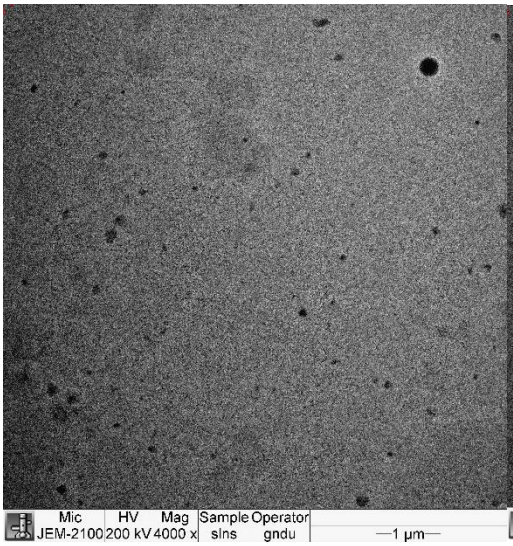

Figure 5

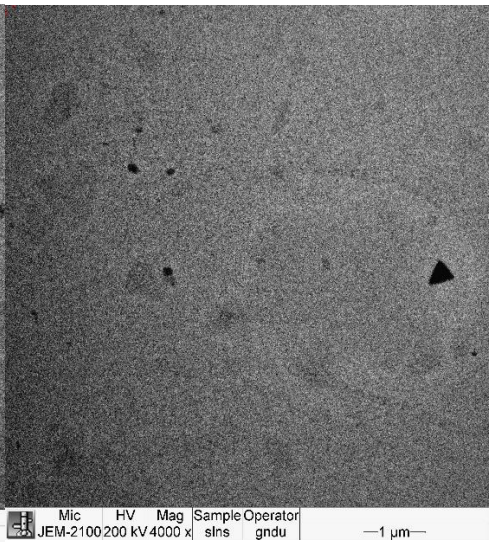

Figure 6

Figure 5.6 TEM images of the MMF-loaded SLNs clearly show the nanoparticles are spherical and have a smooth surface.

7. *In-vitro* drug release study of SLNs dispersions

In-vitro drug release studies for all the SLNs dispersions up to 24 hours was carried out by using dialysis membrane

(molecular cut off 12000 Daltons). The previous studies have reported the role of surfactant can improving the drug release from nanocarrier based system. All the eight formulations contained different compositions of surfactants respectively. The maximum release was found in F8 formulation i.e. (88.25946±25.006%). The formulation F8 having maximum drug release of 80% during 24 hrs (Figure 7).

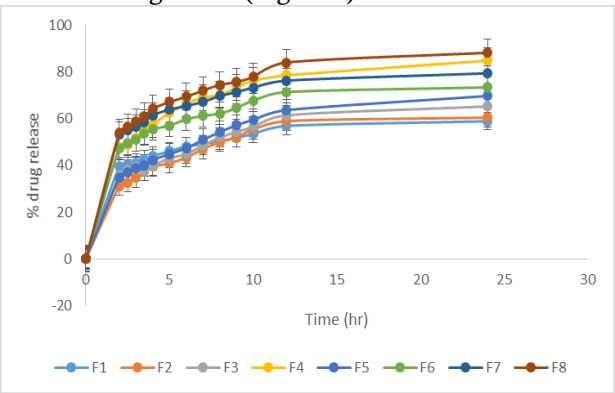

Figure. 7 Comparative in- vitro drug release profiles of SLNs dispersions (mean ±S.D., n=3).

Table 4. shows the release behavior of the different SLN dispersions was analyzed using various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. It was observed that all the prepared SLN dispersions followed both zero-order and first-order kinetics. To determine the best-fitting model, regression analysis was conducted for each kinetic model. Among the formulations, F8 exhibited the highest correlation coefficient (R^2 = 0.8085), suggesting that this model most accurately represents the drug release profile of the MMF formulation.

Table 4.: Kinetic parameters of MMF released from the dispersions:

Formulation code	Kinetic	Correlation (r^2)
F1	First order	0.8083
F2	First order	0.8082
F3	First order	0.8083
F4	Zero order	0.7681
F5	Zero order	0.7493
F6	First order	0.8081
F7	First order	0.8084
F8	**First order**	**0.8085**

7.1 Characteristics of MMF loaded SLN based gel formulations

7.2 Physicochemical properties

The gels were checked visually for their color, uniformity, and texture. A gel base was prepared using 1.5% (w/w) Carbopol 940, which provided the best consistency when combined with the optimized SLN formulation (F8) to create the SLN-based gel. The ingredients and characteristics of this gel formulation are summarized in Table 5.

Formulation code	Carbopol 940 conc (%w/w)	Drug loaded SLNs	Appearance	pH	Spreadability (cm^2)
F1	0.5	F8	Fluidy, Non-greasy	6.3±0.2	7.1±0.3
F2	1	F8	Homogeneous, Greasy	6.5±0.3	7.4±0.5
F3	**1.5**	**F8**	**Creamy, Homogeneous, Non- greasy**	**6.2±0.4**	**7.6±0.4**
F4	2	F8	Stiff mass	6.8±0.4	7.9±0.2

Table 5: Composition and characterization of SLNs based gel formulation

7.3 *In-vitro* drug release study

The *in-vitro* release of MMF from various formulations including an MMF-loaded suspension, MMF-loaded Carbopol gel, and the F3 formulation was evaluated using a dialysis method.The MMF suspension released the drug almost immediately, with about 82.90 ± 1.84% released within 12 hours. In contrast, both the MMF-loaded carbopol gel and the F3 formulation showed a slower and more controlled release. When comparing these two, MMF release from F3 was slower, with only 56.09 ± 33.7% released after 24 hours, compared to 68.11 ± 0.92% from the carbopol gel. These findings align with earlier reports, showed that embedding nanoparticle dispersions within gels can further slow down drug release. This slower release is likely due to the drug being held back by the polymer network in the gel matrix.

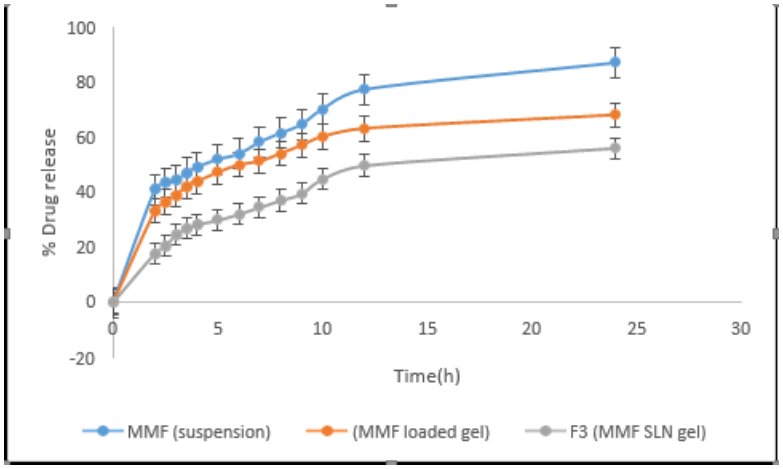

Figure 8. Comparative in-vitro drug release profiles MMF-suspension, MMF loaded gel, and MMF SLN-based gel SLN-based gel

7.4 Release Kinetics: To study how the drug was released over time, different kinetic models were applied, including zero-order, first-order, Korsmeyer-Peppas, Higuchi diffusion, and Hixson-Crowell models, as summarized in Table 6. Among these, the zero-order model provided the best fit, indicated by the highest regression coefficient. Zero order release indicates the release from systems which is not dependent on the amount of substances present.

Kinetic models	Equation	Correlation (r^2)
Zero order	3.227x+5.3521	0.8621
First order	0.2544x+0.4977	0.8083
Korsmeyer-Peppas	0.121x+0.6507	0.4807
Higuchi diffusion	0.0971x+1.1767	0.239
Hixon Crowell	0.7667x- 0.1667	0.6127

Table 6: Kinetic parameters of MMF released from the SLN-based hydrogel

7.5 *Ex-vivo* skin permeation studies

The drug permeation profile of MMF suspension, MMF gel and MMF-SLN based gel are presented in fig 6. It was observed that the steady increase of MMF was achieved from F3 across the epidermis with time. F3 was found to show better permeation as compared to the MMF suspension and gel formulation. The SLN gel possessed sustained drug release over a period of 24 h. In a previous study reported observed the slower release of the drug from the SLN gel formulation over an extended period of time (32). The amount of drug permeated through the skin at the end of 24 hour from MMF-SLN gel formulation was considerably less (34.77±0.13%) as compared to MMF-plain gel formulation (56.76±0.31%) and MMF-suspension formulation (74.98±0.73%) as depicted in Figure 6. According to literature, the most effective topical drug delivery systems are those that minimize drug permeation

through the skin, allowing the highest concentration to remain in the target layers, the epidermis and dermis. In this context, the F3 formulation showed promising results, with the drug evenly distributed throughout the gel matrix and gradually diffusing into the receptor medium. The slow release is likely due to the formation of a true solid solution between the drug and lipid components, which slows down rapid drug release. Additionally, the gel's high viscosity further limits drug release by reducing water penetration into the matrix. These features make the F3 formulation a promising system for delivering high concentrations of the drug directly to the target skin layers, a crucial factor for effectively managing conditions like psoriasis. The permeability data for the MMF suspension, MMF Carbopol gel, and F3 are shown in Table 7. The study evaluated parameters like steady-state flux (Jss) and the permeability coefficient (Kp). After 24 hours, the F3 formulation showed a notably higher drug flux (2.875 ± 0.057 µg/cm²/h; $p < 0.05$) compared to the MMF-loaded Carbopol gel (1.716 ± 0.028 µg/cm²/h) and the plain drug suspension (1.607 ± 0.036 µg/cm²/h), indicating improved drug delivery through the skin. Moreover, the partition coefficient of F3 was also significantly greater than that of the other two formulations. Overall, these results indicate that the SLN-based gel (F3) substantially enhances the permeation and delivery of MMF through the skin, making it a strong candidate for topical therapy.

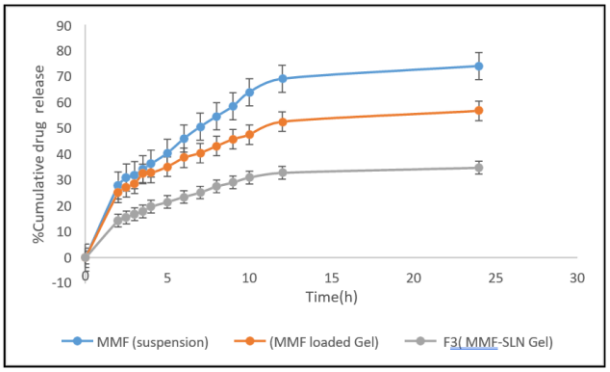

Figure 6: % Cumulative drug release of MMF in gel formulations, MMF-suspension, MMF loaded gel and MMF-SLN-gel (mean ± S.D., n=3).

Table 7. Permeation data of MMF-suspension, MMF-gel and SLN based hydrogel

Parameters	Flux (µg/cm²/h)	Permeability coefficient (cm/s)
MMF-suspension	1.607±0.0036	0.8203± 0.012
MMF- gel	1.716±0.028	0.8682± 0.008
MMF-SLN based hydrogel	2.875±0.057	1.437 ± 0.009

CONCLUSION

The aim of this study was to design and develop nanocarrier systems of MMF for effective treatment of psoriasis. SLNs were selected as carrier for topical delivery due to the desirable characteristics involving nanometric size range, permeability to lower epidermis and somewhat upper dermis, tendency to encapsulate lipophilic drugs and occlusive action. The SLNs containing MMF were prepared by solvent injection method. The preformulation studies were performed for the selection of suitable components and formulation. Various solvents, solid lipids, surfactants and emulsifiers were screened for formulation development based on their solubilising capacity. Different SLN formulations were prepared using solid lipid Precirol ATO5 in varying concentrations of 0.1 to 0.2% respectively. Soya lecithin and Labrasol were used as emulsifier and surfactant, to prepare pharmaceutically stable formulations. Out of the eight formulations developed, the one containing 0.2% Precirol ATO5, 0.03% soya lecithin, and 2% Labrasol (referred to as F8) was selected as the optimized formulation. This selection was based on key parameters such as particle size, zeta potential, polydispersity index (PDI), encapsulation efficiency, and drug content. The optimized F8 formulation had a vesicle size in the nanometre range (199.4 ± 0.8 nm) with a PDI of 0.303 ± 0.008, indicating a fairly uniform size distribution. Its zeta potential was measured at -13 ± 0.008 mV, suggesting good stability. Among all the formulations tested, F8 also showed the highest encapsulation efficiency at 86.9 ± 0.15%. To prepare

a topical delivery system, carbopol-based gels were formulated using varying concentrations of Carbopol 940 (0.5%, 1%, 1.5%, and 2% w/w). The 1.5% w/w concentration was found to be optimal based on parameters like pH (6.8 ± 0.4), physical appearance, and spreadability (7.9 ± 0.2 cm²), and was therefore chosen for further development. The F8 formulation was then incorporated into this carbopol gel base to create a solid lipid nanoparticle (SLN) gel at a concentration of 1.5% w/w. Once the SLN-based hydrogel was successfully prepared and found to be physically stable, it underwent in-vitro drug release studies. An ideal topical formulation should provide a prolonged release profile to minimize frequent application and improve patient compliance. The MMF suspension showed rapid drug release (82.90 ± 1.84%) within 12 hours, while both the MMF-loaded carbopol gel and the SLN-based gel displayed slower, more sustained release. Notably, the SLN gel formulation released the drug more gradually (56.09 ± 33.7%) than the MMF-loaded carbopol gel (8.11 ± 0.92%). An ex-vivo skin permeation study using Franz diffusion cells and Wistar rat skin further evaluated the performance of the optimized SLN gel. This formulation showed significantly improved skin permeation ($p < 0.005$), with a steady-state flux (Jss) of 2.875 ± 0.057 µg/cm²/h and a permeability coefficient of 1.437 ± 0.009, outperforming both the MMF aqueous suspension and the MMF-loaded carbopol gel. These findings suggest that the SLN-based hydrogel could serve as an effective delivery system for the topical treatment of psoriasis. Future studies, including in-vivo evaluations and long-term stability testing, are needed to further validate its potential as a reliable nanocarrier for MMF.

REFERENCES

1. Jeffrey Zwerner, David Fiorentino Dermatologic Therapy, 2007: (20) 229–238) https://doi.org/10.1111/j.1529-8019.2007.00136.x
2. Alsberg CL, Black OF. Contribution to the study of maize deterioration; biochemical and toxicological investigations of Penicillium puberulum and Penicillium stoloniferum. Bull Burl Anim Ind US Dept Agr 1913; 270:1-47
3. Grundmann-Kollmann, M., Mooser, G., Schraeder, P., Zollner, T., Kaskel, P., Ochsendorf, F., Boehncke, W.H., Kerscher, M., Kaufmann, R. and Peter, R.U. (2000). Treatment of chronic plaque-stage psoriasis and psoriatic arthritis with mycophenolate mofetil. Journal of the American Academy of Dermatology, 42(5): 835-837. https://doi.org/10.1067/mjd.2000.104890
4. Zur Mühlen, A., Schwarz, C. and Mehnert, W. (1998). Solid lipid nanoparticles (SLN) for controlled drug delivery–drug release and release mechanism. European Journal of pharmaceutics and Biopharmaceutics, 45(2): 149-155.https://doi.org/10.1016/S0939-6411(97)00150-1
5. Sonawane, R., Harde, H., Katariya, M., Agrawal, S. and Jain, S. (2014). Solid lipid nanoparticles-loaded topical gel containing combination drugs: an approach to offset psoriasis. Expert Opinion on Drug Delivery, 11(12):1833-1847.https://doi.org/10.1517/17425247.2014.938634
6. Aljaeid, B.M. and Hosny, K.M., (2016). Miconazole-loaded solid lipid nanoparticles: formulation and evaluation of a novel formula with high bioavailability and antifungal activity. International Journal of Nanomedicine, 11: 441-447.https://doi.org/10.2147/IJN.S100625
7. Kamble, V., Jagdale, D. and Kadam, V., "Solid Lipid Nanoparticles as Drug Delivery System", International Journal of Pharma and Bio Sciences, 1(3). 1-9. 2010.
8. Kakkar, V., Singh, S., Singla, D. and Kaur, I.P. (2011). Exploring solid lipid nanoparticles to enhance the oral bioavailability of curcumin. Molecular nutrition & food research, 55(3): 495-503.https://doi.org/10.1002/mnfr.201000310
9. Attama, A.A. and Umeyor, C.E., (2015). The use of solid lipid nanoparticles for sustained drug release. Therapeutic Delivery, 6(6):669-684, https://doi.org/10.4155/tde.15.23
10. Garud, A., Singh, D. and Garud, N, "Solid Lipid Nanoparticles Method, Characterization and Applications", International Current Pharmaceutical Journal, 1 (11). 384-393. 2012.https://doi.org/10.3329/icpj.v1i11.12065
11. Varshosaz, J., Ghaffari, S., Khoshayand, M.R., Atyabi, F., Azarmi, S. and Kobarfard, F. (2010). Development and optimization of solid lipid nanoparticles of amikacin by central composite design. Journal of Liposome Research, 20(2): 97-104. https://doi.org/10.3109/08982100903103904
12. Grundmann-Kollmann, M., Mooser, G., Schraeder, P., Zollner, T., Kaskel, P., Ochsendorf, F., Boehncke, W.H., Kerscher, M., Kaufmann, R. and Peter, R.U. (2000). Treatment of chronic plaque-stage psoriasis and psoriatic arthritis with mycophenolate mofetil. Journal of the American Academy of Dermatology, 42(5): 835-837. https://doi.org/10.1067/mjd.2000.104890
13. Sievers, T.M., Rossi, S.J., Ghobrial, R.M., Arriola, E., Nishimura, P., Kawano, M. and Holt, C.D. (1997). Mycophenolate mofetil Pharmacotherapy. The Journal of Human Pharmacology and Drug Therapy, 17(6): 1178-

1197.https://doi.org/10.1002/j.1875-9114.1997.tb03082.x
14. Behrend, M., (2001). Adverse gastrointestinal effects of mycophenolate mofetil. Drug Safety, 24(9):645-663.
15. Zur Mühlen, A., Schwarz, C. and Mehnert, W. (1998). Solid lipid nanoparticles (SLN) for controlled drug delivery–drug release and release mechanism. European Journal of pharmaceutics and Biopharmaceutics, 45(2): 149-155.
16. Sonawane, R., Harde, H., Katariya, M., Agrawal, S. and Jain, S. (2014). Solid lipid nanoparticles-loaded topical gel containing combination drugs: an approach to offset psoriasis. Expert Opinion on Drug Delivery, 11(12):1833-1847 https://doi.org/10.1517/17425247.2014.938634
17. Jain, A.K., Jain, A., Garg, N.K., Agarwal, A., Jain, A., Jain, S.A., Tyagi, R.K., Jain, R.K.,Agrawal, H. and Agrawal, G.P. (2014). Adapalene loaded solid lipid nanoparticles gel: an effective approach for acne treatment. Colloids and Surfaces B: Biointerfaces, 121:222-229.https://doi.org/10.1016/j.colsurfb.2014.05.041
18. Pople, P.V. and Singh, K.K. (2011). Development and evaluation of colloidal modified nanolipid carrier: application to topical delivery of tacrolimus. European Journal of Pharmaceutics and Biopharmaceutics, 79(1): 82-94 https://doi.org/10.1016/j.ejpb.2011.02.016.
19. M, Ahmed OA, Fahmy UA, Ahmed TA. Solid lipid nanoparticles for transdermal delivery of avanafil: optimization, formulation, in-vitro and ex-vivo studies. Journal of liposome research. 2016 Oct 1;26(4):288-96 https://doi.org/10.3109/08982104.2015.1117490.
20. R.H. Müller, S. Heinemann, Fat emulsions for parenteral nutrition. III. Lipofundin MCT/LCT regimens for parenteral nutrition (TPN) with low electrolyte load, Int. J. Pharm. 101 (1994) 175–189 https://doi.org/10.1016/0378-5173(94)90213-5.
21. Agrawal Y, Petkar KC, Sawant KK. Development, evaluation and clinical studies of Acitretin loaded nanostructured lipid carriers for topical treatment of psoriasis. Int J Pharm 2010; 401:93-102 https://doi.org/10.1016/j.ijpharm.2010.09.007
22. Solid lipid nanoparticles for transdermal delivery of avanafil: optimization, formulation, in-vitro andex-vivo studies Mallesh Kurakula, Osama A. A. Ahmed, Usama A. Fahmy & Tarek A. Ahmed 2015 journal of liposome research (1-9) https://doi.org/10.3109/08982104.2015.1117490.
23. Peltola, S., Saarinen-Savolainen, P., Kiesvaara, J., Suhonen, T.M. and Urtti, A. (2003). Microemulsions for topical delivery of estradiol. International Journal of Pharmaceutics, 254(2): 99-107.https://doi.org/10.1016/S0378-5173(02)00632-4
24. Zhu, W.W., Yu, A.H., Wang, W.H., Dong, R.Q., Wu, J., Zhai, G.X., 2008. Formulation design of microemulsion for dermal delivery of penciclovir. Int. J. Pharm. 360,184–190 https://doi.org/10.1016/j.ijpharm.2008.04.008
25. Chawla, V. and Saraf, S.A. (2012). Rheological studies on solid lipid nanoparticle based carbopol gels of aceclofenac. Colloids and Surfaces B: Biointerfaces, 92: 293-298.https://doi.org/10.1016/j.colsurfb.2011.12.006
26. Verma, A., Singh, S., Kaur, R., Kumar, A. and Jain, U.K. (2013). Formulation, optimization and evaluation of clobetasol propionate gel. International Journal of Pharmacy and Pharmaceutical Sciences, 5(4): 666-678
27. Souto, E.B. and Müller, R.H. (2005). SLN and NLC for topical delivery of ketoconazole. Journal of Microencapsulation, 22(5): 501-510.https://doi.org/10.1080/02652040500162436
28. Chadusama, A., Patel, V. and Vasu, K. (2012). Investigation of microemulsion system for transdermal delivery of itraconazole. Journal of Advanced Pharmaceutical Technology and Research, 1: 30-38 doi-10.4103/2231-4040.79802
29. Koelsch, C. (1994). Edible water vapor barriers: properties and promise. Trends in Food Science & Technology, 5(3):76-81https://doi.org/10.1016/0924-2244(94)90241-0
30. Krishnatreyya, H., Dey, S., Pal, P., Das, P.J., Sharma, V.K., Mazumder, B. (2019). Piroxicam Loaded Solid Lipid Nanoparticles (SLNs): Potential for Topical Delivery. Indian Journal of Pharamceutical Education and Research. 53(2): 82-92 doi : 10.5530/ijper.53.2s.52
31. M. H., Han et al., (2007). Topical application of silymarin reduces chemical-induced irritant contact dermatitis in BALB/c mice, International Immunopharmacology. 7: 1651-1658.https://doi.org/10.1016/j.intimp.2007.08.019
32. Menon, S.K., Modi, N.R., Mistry, B., Joshi, K. (2011). Improvement of some pharmaceutical properties of mycophenolate mofetil (MMF) by para sulphonatocalix resorcinarene inclusion complex. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 1:70(1- 2):121-181

