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"DEVELOPMENT AND CHARACTERIZATION OF METFORMIN LOADED MICROSPONGE FOR DUAL ACTION"

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ABSTRACT

The present study was carried out with the aim of development and optimization of multi particulate drug delivery system of Metformin loaded microsponges for controlled drug delivery, targeting diabetes management and localized anti-inflammatory effects. Using the quasi-emulsion solvent diffusion method, microsponges were formulated with ethyl cellulose and Eudragit RS 100 as retardant polymers, and process parameters were optimized through variations in polymer types and concentrations, stirring speeds, and ratios of active pharmaceutical ingredient (API) to polymer for controlled release. Among the formulations, F8 showed the highest drug content (85.57% entrapment efficiency) and sustained in vitro release (87.83%). This optimized formulation was incorporated into a topical gel, exhibiting favourable properties such as ideal viscosity, pH, and spreadability. The findings highlight the potential of Metformin microsponges in achieving dual therapeutic benefits through sustained, localized, and systemic delivery, offering a novel approach for managing diabetic complications.

KEYWORDS: Metformin, Microsponges, Quasi emulsion solvent diffusion, Ethyl cellulose, Eudragit RS 100.

INTRODUCTION

Diabetic foot ulcers (DFUs) are a common and debilitating complication of diabetes mellitus, particularly in patients with longstanding or poorly controlled diabetes.[1] contributing significantly to patient morbidity and healthcare costs. The chronic nature of DFUs and their association with poor wound healing often leads to infections, amputations, and decreased quality of life.[2] The management of diabetic foot ulcers requires a multifaceted approach, involving effective antimicrobial treatment, wound care, and promotion of tissue regeneration. Current treatments for DFUs include systemic antibiotics, wound debridement, and topical therapies, but there remains an urgent need for more effective, targeted therapies to accelerate healing and reduce complications.[3]

Microsponge-based systems are microporous, polymeric particles that can encapsulate active pharmaceutical ingredients (APIs) in their internal network. These systems offer several advantages, including sustained and controlled release of drugs, enhanced stability, and reduced toxicity. Additionally, they can improve patient compliance by reducing the frequency of dosing.[4]

Microsponge drug delivery systems are increasingly preferred over single-unit dosage forms due to their ability to maintain stable plasma drug concentrations, minimize the risk of local irritation at the application site, reduce intra- and inter-subject variability, and enhance bioavailability.[5] Additionally, they can be incorporated into various dosage forms, making them a versatile option for drug delivery.[6]

Metformin, a first-line drug for the management of type 2 diabetes, has been shown to possess anti-inflammatory and wound-healing properties beyond its primary role in glucose regulation.[7] Recent studies have highlighted its potential as an adjunct in the treatment of diabetic foot ulcers, due to its ability to modulate inflammatory responses, enhance cellular regeneration, and promote healing.[8] However, the systemic use of metformin may result in adverse effects, particularly gastrointestinal discomfort, limiting its clinical application for local wound healing. To overcome these limitations, novel drug delivery systems have been developed to enhance the therapeutic profile of metformin. Among these, microsponge drug delivery systems (DDS) have emerged as a promising approach for controlled drug release and targeted action.[9]

Metformin-loaded microsponge systems have the potential to improve its pharmacokinetic properties by maintaining therapeutic drug levels over an extended period, minimizing side effects, and enabling dual action

for glycaemic control and improved patient compliance.[10]

Microsponges, a novel drug delivery system, offer an advanced solution for the targeted delivery of drugs. These small, spherical particles have a unique porous structure that enables the encapsulation of both hydrophilic and lipophilic drugs. Microsponges provide several advantages, including controlled drug release, reduced systemic side effects, and improved stability.[11] When used in topical formulations, such as gels, they allow for localized, prolonged drug action at the site of the ulcer, enhancing the therapeutic outcomes in treating DFUs.

Therefore, the present study carried out with an objective of development and characterization of metformin-loaded microsponge systems for dual action: promoting wound healing in diabetic foot ulcers and exerting anti-inflammatory effects. The study will focus on the optimization of the microsponge formulation it includes, influence of type and concentration of retardant material, drug: polymer ratio, internal phase volume & external phase volume, surfactant concentration, stirring speed, stirring time and then characterization of prepared microsponges.[12]

The microsponge formulation will be incorporated into a gel form for convenient topical application. By encapsulating metformin in microsponges, we intend to provide a controlled release of the drug at the wound site, potentially improving healing outcomes while minimizing systemic exposure and side effects.

MATERIALS AND METHOD

MATERIALS

- Active Ingredient: Metformin hydrochloride (API).
- Polymers: Ethylcellulose and Eudragit RS 100.
- Solvent and Surfactants: Dichloromethane (DCM) for API solubilization and polyvinyl alcohol (PVA) as the stabilizer in the aqueous phase**.**

METHOD

Characterization of pure drug.

a. **Melting point determination:** Capillary method was used for the determination melting point of Metformin. A few crystals of compound are placed in a thin-walled capillary tube of about 10-15 cm long and 1 mm inside diameter and closed at one end. The capillary tube which contains the sample and a thermometer are then suspended in to an oil bath containing liquid paraffin. So, they can be heated slowly and evenly. The temperature range over which the sample is observed to melt is taken as the melting point.[13]

b. **Differential scanning calorimetry:** The DSC of the Metformin was recorded using Du Pont thermal analyzer with 2010 DSC module in nitrogen atmosphere at a heating rate of 10 °C/min.[13]

c. **Calibration curve of metformin in pH 7.4 phosphate buffer:** To determine the wavelength of maximum absorption (λ max), Metformin solution (10 µg/ml) was prepared in distilled water and scanned in UV wavelength of 200- 400nm utilizing the distilled water as a blank solution. The absorption maximum obtained in graph is considered as λ max for the pure drug solution with respective to buffer. 50mg of Metformin was accurately weighed and dissolved in 50ml distilled water in 50ml volumetric flask sonicated for 15 min to get a 1000µg/ml solution. From the stock solution the required working stock solution was prepared to get concentration of 4, 8, 12, 16 and 20µg/ml. then the absorbance was measured at 232nm using UV visible spectrophotometer. The standard graph was repeated for 3 times (n=3). The mean data was plotted by taking the concentration on X-axis and absorbance on Y-axis.[14]

d. **Compatibility studies:** Infrared (IR) spectrometer is the most commonly used non thermal technique for screening of drug-excipients compatibility. This technique provides a unique fingerprint for the drug and the excipients based on their physical and chemical attributes. Weighed amount of drug [Metformin] and other excipients [Ethylcellulose, Eudragit-RS-100] were mixed with IR grade Potassium Bromide (1:10) and compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. The pellet was scanned by IR spectrophotometer over a range of 4000cm^{-1} to 400cm^{-1}.[15]

Preparation of microsponges: Microsponges are prepared by Quasi-emulsion solvent diffusion method which is two-step process. The polymers are dissolved in solvent [Internal phase]. Then drug is added into the solution and dissolved by using ultra sonication at 35°C. The Internal phase was poured drop by drop to External phase which contains distilled water and polyvinyl alcohol (PVA). Continuous stirring with hot plate magnetic stirrer then filters the above and dried in hot air oven at 40°C.The formed microsponge was kept in air tight container for further studies.[16]

Table 1: formulation design for microsponge preparation.

Batch	Drug to Polymer ratio	Type of Internal phase	Volume of Internal phase volume (mL)	Volume of External phase volume (mL)	Surfactant conc. (%)	Stirring speed (R.P.M)	Stirring time (mins)
INFLUENCE OF TYPE AND CONCENTRATION OF RETARDENT MATERIAL							
F1	1:1 (EC)	Ethanol + DCM	20	50	0.75	1500	60
F2	1:2	Ethanol + DCM	20	50	0.75	1500	60
F3	1:3	Ethanol + DCM	20	50	0.75	1500	60
F4	1:1 (Eudragit)	Ethanol + DCM	20	50	0.75	1500	60
F5	1:2	Ethanol + DCM	20	50	0.75	1500	60
F6	1:3	Ethanol + DCM	20	50	0.75	1500	60
INFLUENCE OF DRUG: POLYMER RATIO							
F1	1:1	Ethanol + DCM	20	50	0.75	1500	60
F7	3:1	Ethanol + DCM	20	50	0.75	1500	60
F8	5:1	Ethanol + DCM	20	50	0.75	1500	60
INFLUENCE OF INTERNAL PHASE VOLUME							
F9	5:1	Ethanol + DCM	10	50	0.75	1500	60
F8	5:1	Ethanol + DCM	20	50	0.75	1500	60
F10	5:1	Ethanol + DCM	30	50	0.75	1500	60
INFLUENCE OF EXTERNAL PHASE VOLUME							
F11	5:1	Ethanol + DCM	20	40	0.75	1500	60
F8	5:1	Ethanol + DCM	20	50	0.75	1500	60
F12	5:1	Ethanol + DCM	20	60	0.75	1500	60
INFLUENCE OF SURFACTANT CONCENTRATION							
F13	5:1	Ethanol + DCM	20	50	0.5	1500	60
F8	5:1	Ethanol + DCM	20	50	0.75	1500	60
F14	5:1	Ethanol + DCM	20	50	1.0	1500	60
INFLUENCE OF STIRRING SPEED							
F15	5:1	Ethanol + DCM	20	50	0.75	1000	60
F8	5:1	Ethanol + DCM	20	50	0.75	1500	60
F16	5:1	Ethanol + DCM	20	50	0.75	2000	60
INFLUENCE OF STIRRING TIME							
F17	5:1	Ethanol + DCM	20	50	0.75	1500	30
F8	5:1	Ethanol + DCM	20	50	0.75	1500	60
F18	5:1	Ethanol + DCM	20	50	0.75	1500	120

Evaluation of microsponges[17,18]

Determination of production yield

The production yield of the microsponges was determined by calculating accurately the initial weight of the raw materials and the final weight of the microsponges obtained.

$$Production\ yield = \frac{Practical\ mass\ of\ microsponges}{Theoritical\ mass} \times 100$$

Surface morphology studies: SEM analysis was done on the optimized microsponges' exterior morphology. The powders were imaged by a scanning electron microscope (SEM) run at an accelerating voltage of 10kV using Hitachi SU 3500. The powder in few µg were fixed on to stub by a double-sided sticky carbon tape and kept inside the SEM chamber and analysed at different magnification such as 60X, 200X, 500X, 1.10X and 2.50X respectively to obtain better clarity on the particle morphology/ topology.

Particle size distribution: Measurement of the particle size distribution and mean diameter of microsponges was carried out with an optical microscope. Stage micrometer was used to calculate the eye piece micrometer. 10 deviation of stage micrometer was matched with the deviation of eye piece micrometer and calibration factor was calculated. The particle size was calculated by multiplying the number of the deviation of the eye piece micrometer occupied by the particle with calibration factor. 30 randomly chosen microsponges taken to measure their individual size.

Entrapment efficiency: A sample of dried microsponges equivalent to 10 mg was taken into mortar and pestle and add little amount of phosphate buffer of pH 7.4 and allowed to stand for 24 h. Then transfer content into 100 ml volumetric flask and make up volume to 100 ml with phosphate buffer of pH 7.4. The solution was filtered through Whatman filter paper No.41). From the resulting solution take out 1 ml transferred into 10 ml volumetric flask and then make up the volume to 10 ml by using same solvent. Entrapment

efficiency was determined by UV spectrophotometer at 232 nm.

$$Entrapment\ efficiency = \frac{Actual\ drug\ content}{Theoritical\ drug\ content} \times 100$$

Drug content: Metformin content in microsponges was assayed by an UV spectrophotometric method. Microsponges equivalent to 10 mg of drug were dissolved in a 10 ml of methanol. After suitable dilution absorbance was measured by UV spectrophotometer against blank at Amax 232 nm and drug content was calculated.

In vitro release study: *In vitro* release pattern of microsponges was carried out in dissolution apparatus USP Type-I (basket type dissolution apparatus) using phosphate buffer pH 7.4 as dissolution medium with a modified basket consisted of 5µm of stainless-steel mesh. Microsponges equivalent to 500 mg of drug was taken in the basket. The speed of the rotation is 50 rpm and temperature of 37± 0.5°C. At fixed intervals, aliquots 5 ml sample were withdrawn periodically and were replaced by fresh buffer. The samples were assayed by UV spectrophotometer at 232 nm using phosphate buffer pH 7.4 as blank and % CDR was calculated and plotted against time.

Preparation of Microsponge loaded Capsule[19]

For preparing microsponge capsule,641mg of microsponge equivalent to 500mg of Metformin was filled in hard Gelatin capsule of size-00.

Evaluation of capsule filled with optimized microsponge formulation

In Vitro release study [20]

Capsule filled with optimized microsponge formulation (F8), that is about 641.02mg of microsponge equivalent to 500mg of drug was added to 900ml of pH buffer 7, 4 with USP Type-II (Paddle type dissolution apparatus). The speed of the rotation is 50 rpm and temperature of 37± 0.5°C. At fixed intervals, aliquots 5 ml sample were withdrawn periodically and were replaced by fresh buffer. The samples were assayed by UV spectrophotometer at 232 nm using phosphate buffer pH 7.4 as blank and % CDR was calculated and plotted against time.

Preparation of Microsponge loaded Gel[21]

Step 1 - 1% w/v of Carbopol 934 was dissolved in 100ml of water, kept it in refrigerator for overnight.

Step 2 - With continuous stirring add 1.28g (equivalent to 998.44mg of drug) of microsponge to the above dispersion then, add triethanolamine dropwise to adjust pH 5.5-6.5.

Step 3 - Finally, Methyl Paraben was added to the gel with continuous stirring till it get dispersed in gel completely.

EVALUATION OF MICROSPONGE GEL FORMULATION[22-25]

Physical characteristics: The gels were inspected visually for its colour, clarity, consistency, spreadability.

pH measurement: The pH of microsponge formulation was determined by using digital pH meter.1gm of gel was dissolved in 100ml of distil water and it was placed for 2hr. the measurement of pH of each formulation was done in triplicate and average values were calculated.

Spreadability: For the determination of spreadability, excess of sample was applied in between two glass slides and was compressed to uniform thickness by placing 125g weight for 5 min. weight (1 g) was added to the pan. The time in which the upper glass slide moves over to the lower plate was taken as measure of spread ability.

$$Spreadability = \frac{M \times L}{T}$$

Where, M = Weight tied to the upper slide
L = Length moved on the glass.
T = Time Taken.

Clarity: All developed gels were tested for homogeneity by visual inspection after the gels were set in the container and also for presence of any aggregate.

Viscosity measurement: Brookfield viscometer was used for viscosity determination. The formulation (10g) was taken and it was allowed to calibrate for 5min before measuring the dial reading using spindle no 64 at 20rpm.

In-vitro drug diffusion study of the prepared gel: The diffusion medium used was Phosphate buffer pH 7.4, carried out using Franz diffusion cell. The diffusion cell was placed on the magnetic stirrer; the outlet of the reservoir was maintained at 37±0.5ºC. The receptor compartment was filled with Phosphate buffer pH 7.4, prehydrated cellophane paper was used as the membrane to that add 0.6g gel containing an equivalent dose of 500 mg Metformin microsponge was placed on it. The speed of the stirrer was kept constant. With the help of pipette 2ml of sample was taken for specified period of time.

RESULT AND DISCUSSION

Characterization of pure drug.

Melting point determination[26]

The Metformin melting point was found to be 220℃ by Thiel's tube method and 218℃ by DSC, demonstrated a sharp endothermic peak of Metformin, thus indicating the purity of the drug. The melting point range of Metformin was 220-226℃ indicating crystalline nature of drug.

Determination of λ max[27]

The λ-max of Metformin was determined as stated in Fig 5.11. The absorption spectrum of pure drug was scanned between 400-800 nm with 10µg/ml concentration phosphate buffer pH 7.4 using UV Spectrophotometer.

The maximum peak was obtained at 232 nm that was taken as λ-max.

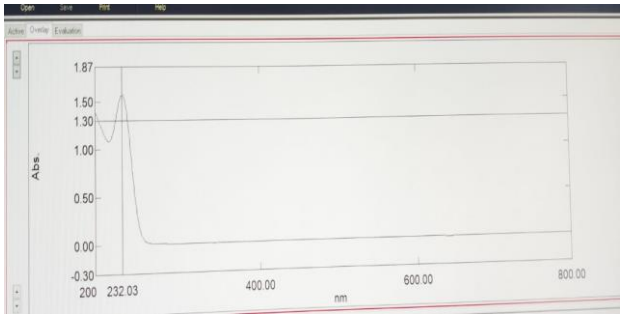

Figure 1: Determination of λ max of 10µg/ml concentration of pure drug.

Standard calibration curve of Metformin: Metformin obeys Beer's law in the concentration range of 4 - 20 µg/ml in phosphate buffer pH 7.4. The regression coefficient (r2) of 0.9949 and slope (m) of 0.0855. the constructed plot of the calibration curve was shown in Figure and confirmed the linearity**.**

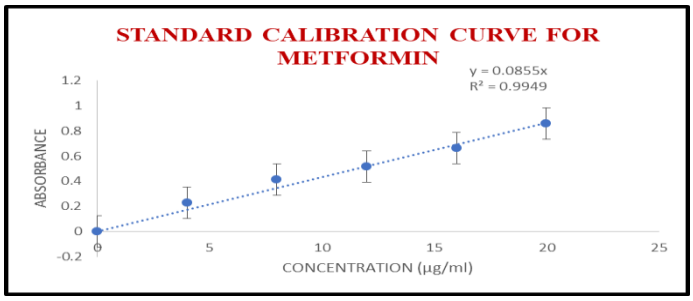

Figure 2: Standard calibration curve for metformin.

Compatibility study by FT-IR Study.

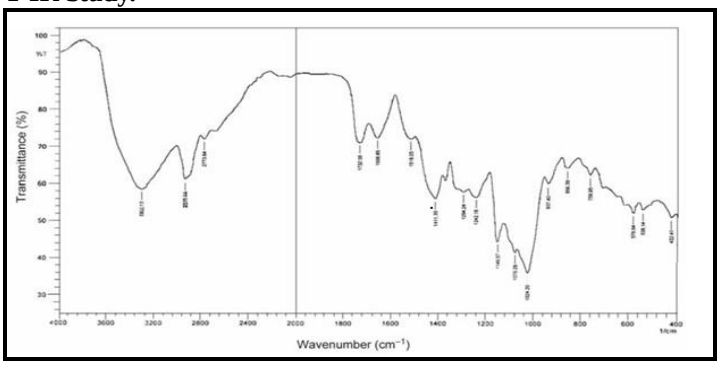

Figure 3: FT IR Spectra of Pure drug (Metformin).

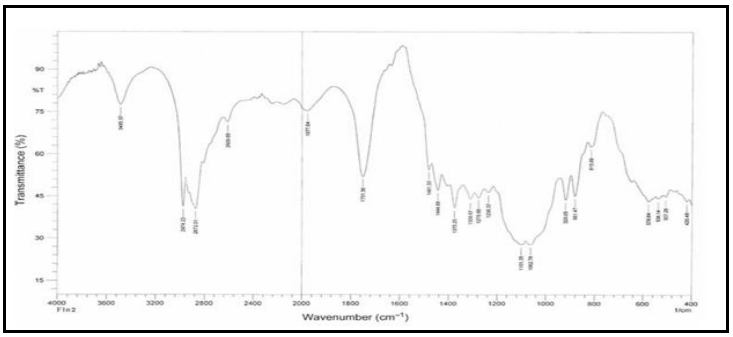

Figure 4: FT IR spectra of optimized formulation.

CHARACTERIZATION OF MICROSPONGE

The metformin loaded microsponges are prepared by quasi emulsion solvent diffusion method. Then, the formulated microsponges are evaluated by the following parameters.

Determination of production yield.

Table 2: Representation of production yield of different formulation (F1-F18).

FORMULATION CODE	(%) PRODUCTION YIELD
F1	61.41
F2	66.86
F3	74.13
F4	58.23
F5	59.04
F6	65.73
F7	63.86
F8	74.20
F9	78.14
F10	63.73
F11	78.14
F12	63.73
F13	63.91
F14	79.61
F15	78.39
F16	60.86
F17	76.43
F18	59.73

Scanning electron microscopy of Microsponge.

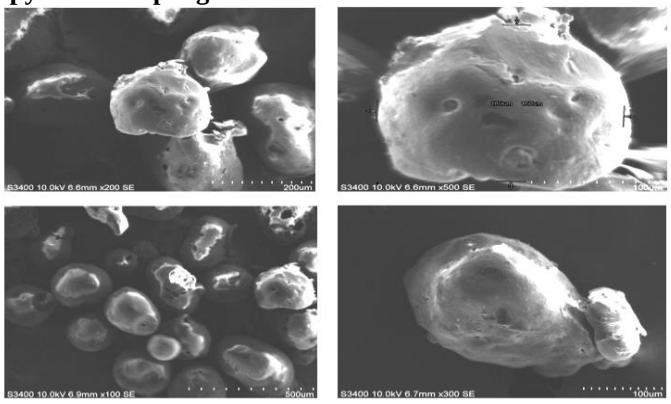

Figure 5: SEM images of optimized formulation.

Determination of particle size

Table 4: Representation of particle size of different formulation (F1-F18).

FORMULATION CODE	AVERAGE PARTICLE SIZE (µm)
F1	50.01
F2	54.62
F3	62.32
F4	45.18
F5	48.14
F6	55.98
F7	38.12
F8	32.36
F9	53.88
F10	30.49
F11	28.19
F12	38.42
F13	39.82
F14	22.29
F15	78.39
F16	30.86
F17	38.19
F18	29.08

Determination of drug content and entrapment efficiency.

Table 5: Representation of % Drug content and % Entrapment efficiency of different formulation (F1-F18).

FORMULATION CODE	(%) Drug content	(%) Entrapment efficiency
F1	68.33	43.99
F2	36.39	61.67
F3	23.09	77.92
F4	58.14	40.72
F5	24.43	59.75
F6	16.67	75.17
F7	80.11	85.26
F8	85.57	87.83
F9	88.49	88.03
F10	73.84	63.14
F11	87.24	88.72
F12	76.32	78.05
F13	73.61	82.37
F14	88.03	88.92
F15	73.29	79.22
F16	86.93	89.22
F17	76.92	76.92
F18	87.86	88.84

In vitro drug release

a. Effect of type and concentration of Retardant materials[28]

Ethyl cellulose was selected as retardant material polymer as it yielded more microsponges with higher % drug content, drug loading and % cumulative drug release. Irrespective of polymer type, increase in concentration of retardant polymer, there was increase in % yield, particle size and % loading efficiency, this is due to greater availability of the retardant material. However, there was decrease in drug content and % cumulative drug release, this might be due to the slow diffusion of the internal phase into the external medium. As ethyl cellulose to drug in 1:1 ratio has resulted in microsponges with acceptable entrapment efficiency, higher drug content and % cumulative drug release. Therefore, it was considered optimum for further studies.

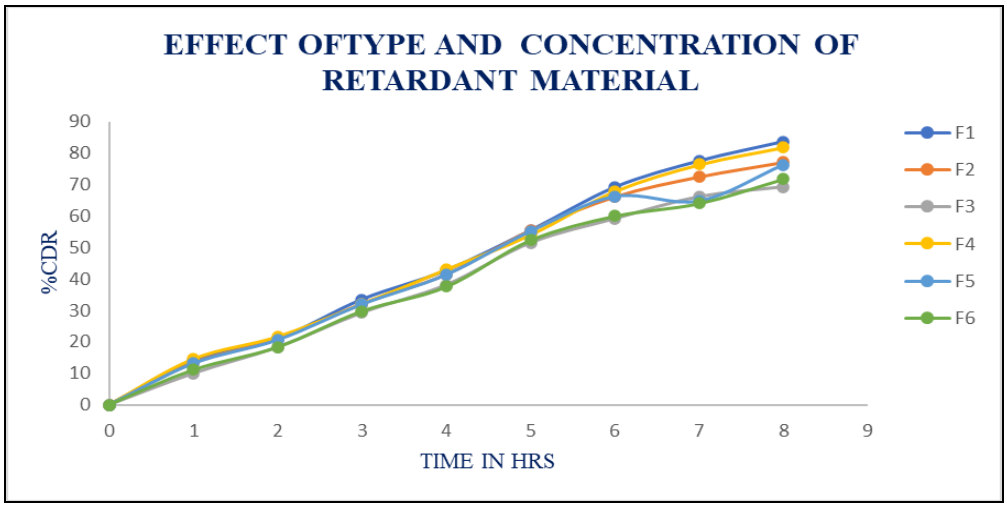

Figure 6: Graphical representation of % CDR on an Effect of type and concentration of retardant material.

b. Effect of Drug to Polymer ratio[29]

An increase in the drug to polymer ratio from 3:1 to 5:1 has resulted in increased drug content, entrapment efficiency and % cumulative drug release. This could be due to increase in the concentration of drug. The Percentage of entrapment efficiency grew progressively until the drug to polymer ratio reached a ratio of 5:1, and there was no additional rise in the percentage of entrapment efficiently. Hence, preparation was ceased at the ratio 5:1. F8 formulation considered for further studies. When the drug to polymer ratio is increased, the mean particle size falls. As the amount of drug increased, the drug content, entrapment efficiency, %Yield and % Drug release gradually increased. This might be due to increased viscosity and faster diffusion of internal phase of the emulsion system.

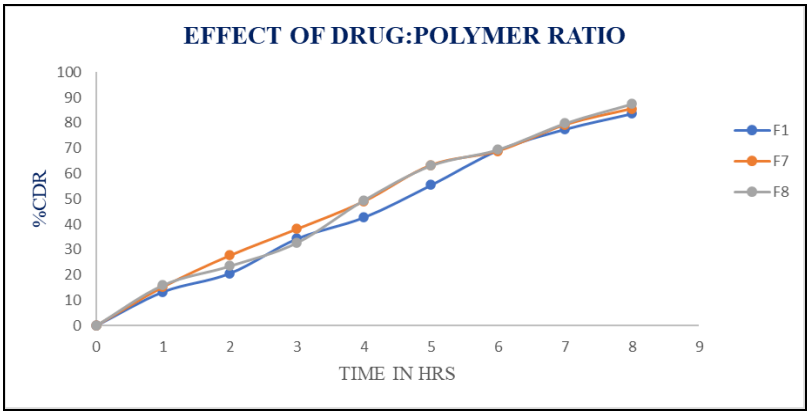

Figure 7: Graphical representation of % CDR on an effect of drug to polymer ratio.

c. Effect of Internal phase volume[30]

The selection of Internal phase volume at different concentration as it greatly affects the particle size due greater viscosity of the internal phase. As it also slightly affects %yield, %EE, drug content and %drug release. As the volume of internal phase increased, %EE and drug content decreased. This is due to, dilution of drug in the increased internal phase volume. The mean particle size decreases as internal phase volume increases. It could be due to greater viscosity of the internal phase with increased volume. As smaller the particle size, the drug release increases, because increased surface area of the particles.

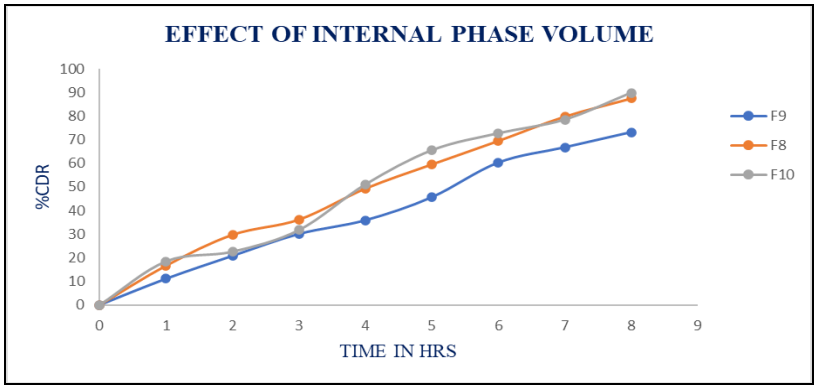

Figure 8: Graphical representation of % CDR on an effect of internal phase volume.

d. Effect of External phase volume[31]

The volume of external phase is critical for the development of microsponges as they lower the free drug concentration. It also affects drug content, %EE, particle size and drug release. An increase in the volume of the external phase liquid there is an increase in the particle size, due to greater viscosity of internal phase globules. Increased volume of external phase results in development of microsponges with lesser drug content and also entrapment efficiency. This is because the drug is more is exposed to aqueous environment of external phase, which results in less effective entrapment in microsponges and reduced % drug release.

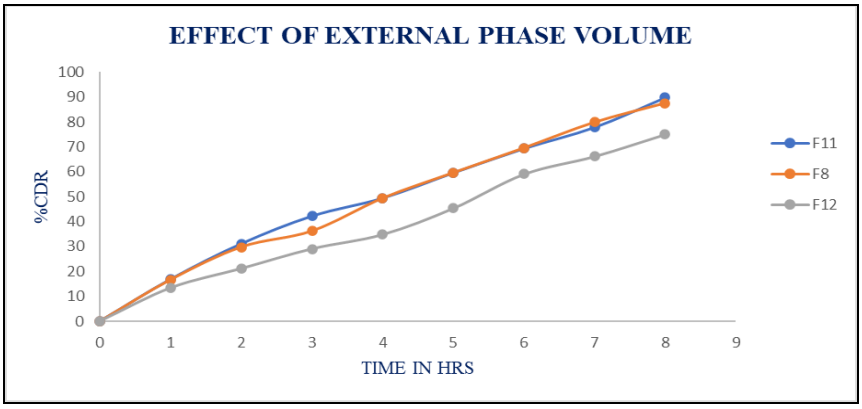

Figure 9: Graphical representation of % CDR on an effect of External phase volume.

e. Effect of concentration of Surfactant[32]

The surfactant concentration plays an important role in the formation of microsponge and they raising the free drug concentration. As 0.75 has considered as optimal concentration for formation of microsponges. Increases in concentration of Surfactant has reduced the particle size due to reduced interfacial tension between the globules and external phase. Upon increase in the surfactant concentration as it increases in the drug content, %yield, %EE and drug release is due to increased solubility of drug.

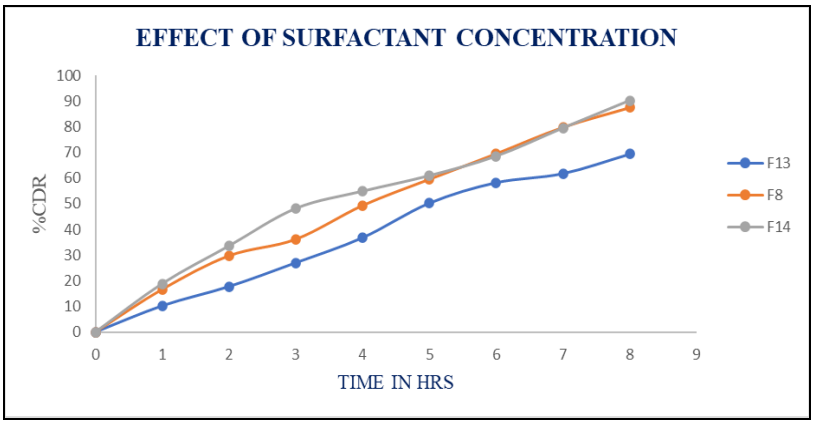

Figure 10: Graphical representation of % CDR on an effect of surfactant concentration.

f. Effect of Stirring speed and time[33]

The stirring speed and time play a crucial role in the development of microsponges, mainly effects on the particle size, the stirring had same effect on the %EE and drug content. By varying Stirring speed of 1500RPM and time 60 minutes was considered as an optimal speed and time for preparation of microsponges. The production yield was decreased by increasing the stirring speed and time because the intense turbulence induced in the external phase caused the polymer to stick to containers. The strong mechanical shear by increasing the stirring speed and time produce the smaller droplets which decrease the mean particle size. Increase in the stirring speed and time increases the %EE and drug content due to improved solubility of drug. Increase in the % drug release is due to larger surface area enhanced by smaller particles.

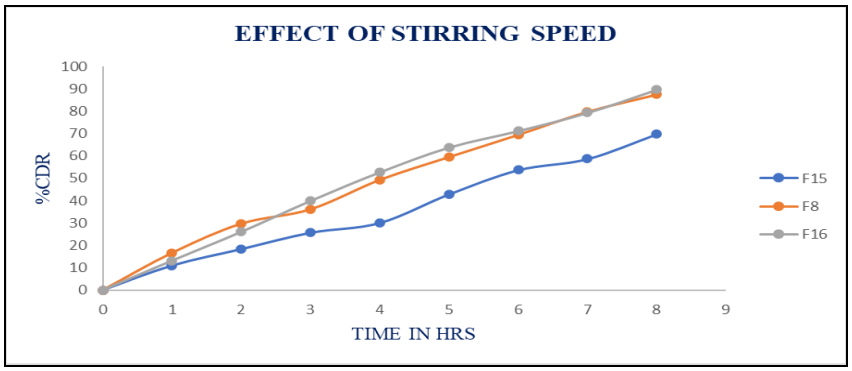

Figure 11: Graphical representation of % CDR on an effect of Stirring speed concentration.

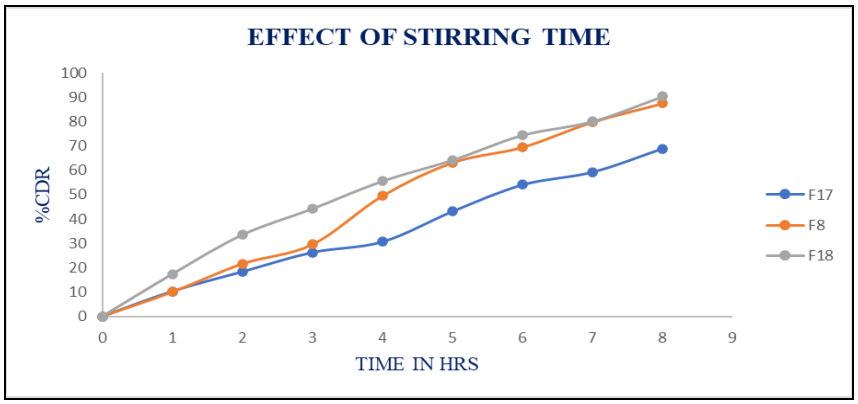

Figure 12: Graphical representation of % CDR on an effect of stirring time.

In Vitro Drug Release of microsponges.[34]

The in vitro drug release studies demonstrated controlled and sustained release over a period of 8 hours for most formulations. For example, formulation F9 showed a cumulative drug release of 73.17% after 8 hours, while F8 demonstrated a superior release profile with 87.53%. These findings highlight the effectiveness of the microsponge system in providing a sustained release mechanism, which is critical for maintaining therapeutic drug levels over time and reducing the frequency of administration.

Stability studies: Stability studies were performed according to ICH guidelines. The optimized formulations were selected for stability studies. They were subjected to short-term stability studies. Formulation was divided into 2 sets of samples and stored at 5±3°C in the refrigerator and stored at room temperature (30°±2°C, 65%±5%RH), and their % Drug content and *In vitro* release were determined after 3 months.

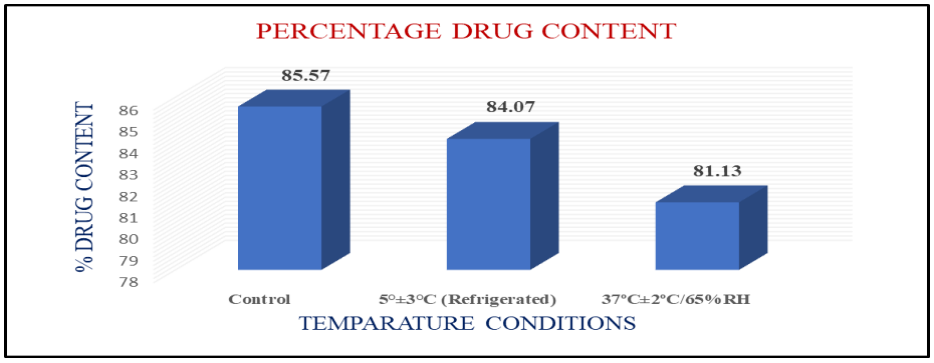

Figure 13: Bar graphical representation of percentage of drug content onstability study.

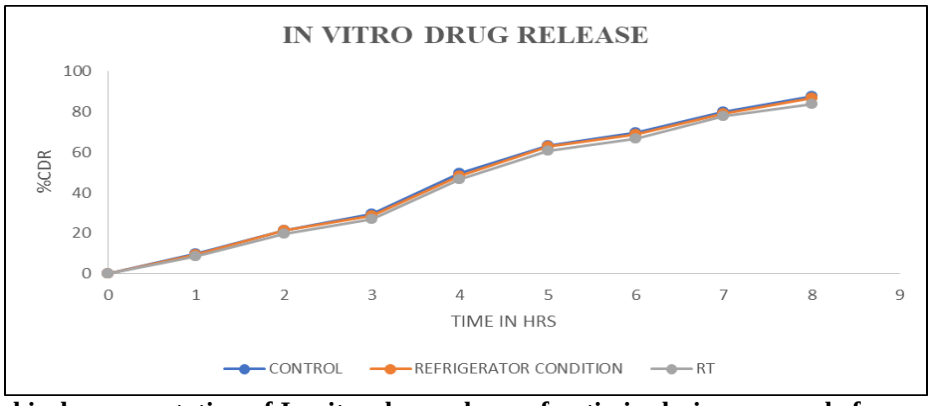

Figure 14: Graphical representation of In-vitro drug release of optimizedmicrosponge before and after 30 days of stability days.

Evaluation of capsule[35]

***In vitro* drug release of Capsule:** The in vitro drug release study of the capsule formulation demonstrated a consistent and sustained release of metformin over a 12-hour period. The cumulative drug release reached 91.04% after 12 hours, with a significant release of 57.13% observed at the 6-hour mark, indicating effective controlled release of the drug.

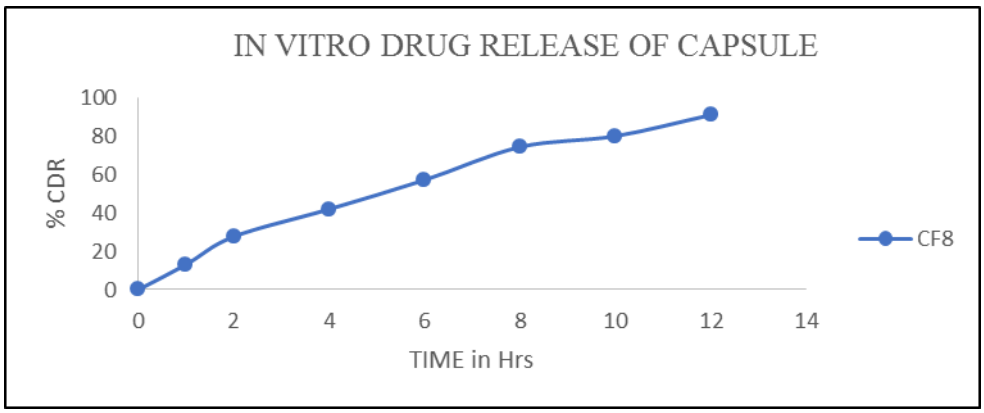

Figure 15: Graphical representation of in vitro drug release of capsule.

Evaluation of Microsponge Gel[36]

Physical appearance: The physical appearance of Metformin loaded microsponge gel formulation was checked and showed colourless, opaque, odourless with smooth appearance.

Physical appearance of formulation was checked and the results are given below table.

Table 6: Physical appearance of the Optimized Microsponge Gel.

FORMULATION	APPEARANCE
F8-G	Colourless, opaque, odourless with smooth appearance

pH measurement: The prepared Metformin loaded microsponge gel was checked for their pH. The formulation was showing pH in the range of 6.2±0.006. This is well in the range of topical administered formulation respectively.

Viscosity: The viscosity of prepared gel formulation was showed 1143±2 respectively. It meets as per the standards. Thus, the gel viscosity ensures good characteristics of the formulation.

Spreadability: The values of spreadability indicate that the gel was easily spreadable by small amount of shear. One of the criteria for a gel to meet the ideal quantities is that it should possess good spreadability. Spreadability of the formulation was found to be 7.2±0.33 g.cm/sec indicating spreadability of drug loaded microsponge gel was good.

Table 7: pH, Viscosity (cps), and Spreadability of optimized microsponge gel.

Formulation code	pH	Viscosity (cps)	Spreadability (g.cm/sec)
F8-G	6.2±0.006	1143±2	7.2±0.33

In Vitro Diffusion Study of Gel Formulation: The in vitro diffusion study of the gel formulation showed a cumulative drug release of 74.15% after 8 hours. The zero-order kinetic model best described the release mechanism, indicating a constant drug release rate. This sustained release profile suggests that the microsponge gel can be an effective topical treatment option, offering prolonged drug action and enhanced patient compliance.

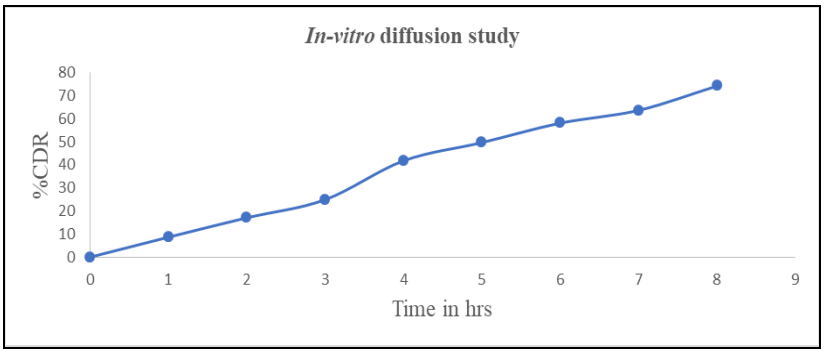

Figure 5.16: Graphical representation of In-vitro diffusion study of optimized microsponge gel.

CONCLUSION

Our research focused on the successful development and optimization of Metformin-loaded microsponges using the quasi-emulsion solvent diffusion method, followed by their evaluation and incorporation into a gel formulation and filled into a Hard Gelatin capsule. The study demonstrated that by optimizing various formulation parameters, such as the concentration of polymers, surfactants, internal and external phase volumes, and stirring conditions, the desired drug release profiles and physical characteristics of microsponges could be achieved. Firstly, successfully developed Metformin-loaded microsponges using the quasi-emulsion solvent diffusion method, demonstrating their potential for controlled and sustained drug release. The Preformulation studies confirmed the purity and proper calibration of Metformin, and various formulation parameters—such as polymer concentration, drug-to-polymer ratio, internal and external phase volumes, and surfactant concentration were optimized to enhance the microsponge characteristics, including drug content, entrapment efficiency, and release profile.

The microsponges showed favourable production yields, drug content, and entrapment efficiency, with smaller particle sizes resulting in faster drug release due to increased surface area. The in vitro drug release studies revealed sustained and controlled release over an 8-hour period, governed predominantly by zero-order kinetics. This confirmed the microsponges' capability to maintain a steady release rate, which is crucial for prolonged therapeutic action and improved bioavailability. Upon incorporation into a gel formulation, the Metformin-loaded microsponges retained their efficacy, as

evidenced by favourable physical properties such as pH, viscosity, and spreadability. The gel demonstrated a consistent and sustained drug release over 8 hours, making it suitable for topical application with prolonged therapeutic effects. The formulation integrated a stability under various storage conditions, though slight degradation was observed at higher temperatures.

Overall, the study concludes that microsponge-based drug delivery systems are a promising approach for improving the controlled release and bioavailability of Metformin. The gel formulation developed offers an efficient and stable means of delivering Metformin topically, which could enhance patient compliance and therapeutic outcomes.

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