# "Formulation and optimization of ornidazole loaded microsponge for vaginal drug delivery "

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**Abstract:**
The aim of the present study is to formulate, development and characterization the Ornidazole microsponge by using Ethyl cellose by quasi emulsion solvent diffulsion method. Microsponge was made target specific release of the drug for vaginal drug delivery.
Materials: Microsponge containing Ornidazole, Ethyl cellulose and PVA used for microsponge preparation. Different stirring rate i.e 500, 800, 1000, 1200 rpm used for preparation.
Objective: Particle size of prepared microsponge was observed by different method. The production yield, entrapment efficiency and drug content were found to be above 70%. The impact of Drug: Polymer ratio and process variables i.e stirring speed and stirring time on the physical features of microsponges like production yield, mean particle size, entrapment efficiency were examined. It was shown that production yield, drug content and entrapment efficiency was found to be change with drug: polymer ratio.
Result: As the polymer concentration increased, thus increasing the thickness of the wall of the polymer matrix which lead to extended diffusion path and ultimately to lesser drug release or more sustained release. The effect of stirring rate on the morphology of micro sponge.
Conclusion: The dispersion of the drug and polymer within the aqueous phase was found to be dependent on the agitation speed. As the speed was increased the size of microsponges was reduced and the microsponges were found to be spherical and uniform.

**Keywords:** Ornidazole, Vaginal drug delivery, Quasi- emulsion solvent diffusion, Ethyl cellulose.

## 1. INTRODUCTION : [1-5]

Recently, there has been a growing recognition that the benefits of intravenous drug infusion can be closely duplicated, without its inconvenience and hazards, by using the oral route as a part of drug administration to provide continuous drug delivery into the systemic circulation.
Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Such products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. When compared to the Microsponge system these can prevent excessive accumulation of ingredients within the epidermis and the dermis. Potentially, the Microsponge system can reduce significantly the irritation of effective drugs without reducing their efficacy. [1]

The modified dosage forms have been developed due to following limitation of conventional drug products:

- Poor patient compliance; increased chances of missing the dose of a drug with short half-life for which frequent administration is necessary.
- A typical peak valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
- The unavoidable fluctuation in the drug concentration may lead to under medication or overmedication as the steady state concentration values fall or rise beyond the therapeutic range. [1]
  The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index whenever overmedication occurs.
- Non site specificity **.**
  Continuous intravenous administration at a programmed rate of infusion has been recognized as the superior mode of drug delivery not only to bypass hepatic "first pass" elimination, but also to maintain a constant, prolonged and therapeutically effective drug level in the body. However, this method of drug delivery entails certain risks and therefore necessitates a close medical supervision of the drug therapy. [2]

The biological effects of drug are determined by many factors, which are strongly influenced by the chemistry of the drug compound. Some research work in drug development has shown that the chemical modification of the parent compounds

can alter the physic chemical properties of the drug and will affect its absorption, distribution and excretion. This approach for the new drug delivery designs has been termed as latentiation. Most drug compounds are not inherently long-lasting in the biological system and require multiple daily dosing to achieve the desired therapeutic results. The effects of pharmaceutical ingredients and formulation designs on the biological activity of the drug have been reviewed extensively in various scientific studies. [3]

An ideal dosage regimen in the drug therapy of any disease is the one which immediately attains the desired therapeutic drug concentration at the site of action in a constant manner. This is possible through the oral administration of conventional dosage forms in particular dosing intervals throughout the drug therapy.[4] To overcome the inconvenience of multiple dosing, the controlled release or sustained release drug delivery systems have been increasingly gaining popularity in the treatment of various diseases. Such drug formulation designs offer the advantage of conveniently delivering the drug to the systemic circulation and also maintain the desired drug blood levels for an extended period of time with a single oral dose . The controlled release dosage forms are not only capable of maintaining drug therapeutic levels with a narrow fluctuation range, but they make it possible to significantly reduce the frequency of drug administration. [2]
Consider the single dosing of a hypothetical drug that follows a simple pharmacokinetic model for disposition. Depending on the route of administration, a conventional dosage form of the drug, e.g., a solution, suspension, capsule, tablet, etc., It can be seen from this figure that administration of a drug by either intravenous injection or an extra-vascular route, e.g., orally or intramuscularly, does not maintain drug delivery systems have been gaining popularity in treating diseases, mainly because of their advantage of maintaining the desired drug blood levels for an extended period of time after a single dose administration .

Topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes. The main advantage of topical delivery system is to bypass first pass metabolism. Avoidance of the risk and inconvenience of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes, gastric emptying time are other advantage of topical preparations.
Ointments are often aesthetically unappealing due to greasiness and stickiness which often result into lack of patient compliance. These vehicles require high concentrations of active agents for effective therapy because of their low efficiency of delivery system, resulting into irritation and allergic reactions in significant users. Other drawbacks of topical formulations are uncontrolled evaporation of active ingredient, unpleasant odor and potential incompatibility of drugs with the vehicles.[4]
Release of active ingredient from conventional topical formulation over an extended period of time is quite difficult . These vehicles require high concentration of active agents for effeciecy of delivery system, resulting into irritation and allergic reaction in significant users.

**1.1 CONTROLLED RELEASE DRUG DELIVERY SYSTEM [1] :**

The history of the controlled-release drug delivery systems is not very old. The development of this advanced technology in designing the drug delivery system spans over four decades. An ideal controlled drug delivery system is the one which delivers the drug at a predetermined rate, locally or systematically, for a specified period of time.

One of the first practically used controlled release oral dosage forms was the spansule capsule, which was introduced in the 1950s. Since then, numerous products based on different mechanisms have been developed. Over the years, many terms and abbreviations as controlled release (CR), extended releas (ER), prolonged action (PA), sustained release (SR), and sustained action (SA) have been used by the manufacturers to describe the product types and features. Although these terms often have been used interchangeably, individual products bearing these descriptions may differ in design and performance. Lately, a variety of nicotine transdermal patches were marketed to help people quit smoking. Technique for controlled release of medicine must be the most basic and very important factor for drug delivery system. Recently, the solid dispersion technique has been used as one of the pharmaceutical methods for controlling medicine release.
Advantages of the Controlled Drug Delivery System [3] :

- Improvement of patient convenience and compliance
- Release drug with a small therapeutic window at a desired constant rate
- Allow drug with a short half-life to act for a desired period of time
- Reduction in fluctuation of steady-state blood levels
- Increased safety margin for high potency drugs
- Maximum utilization of drug (usage of less total drug)
- Reduction in local or systemic side effects
- Improvement in the treatment efficiency
- Reduction in health care cost

Industrial benefits of the Controlled Drug Delivery System:

- Respond to the challenges from generic product and increase patent life by reformulating the drug delivery system which offers better performance
- Convert going off-patent drugs to Over-The-Counter (OTC) drugs to respond to the increasing purchase volume and offset price decrease
- Cut the costs involved in drug discovery by utilizing drug delivery systems that increase the number of potentially viable drug candidates.

**1.2 Microsponge [5] :**

Microsponge technology has become highly competitive and rapidly evolving. More and more developments in delivery systems are been carried out and are being optimized for the efficacy and cost-effectiveness of the therapy.

The Microsponge Delivery System (MDS) is a unique technology for the controlled release of topical agents and consists of macro porous beads, typically 10–25 nm in diameter, loaded with active agent. When applied to the skin, the MDS releases its active ingredient on a time mode and also in response to different stimuli like rubbing, temperature, pH, etc. MDS technology is being used currently in cosmetics, over-the-counter (OTC) skin care, sunscreens and prescription products.

Microsponge technology offers entrapment of ingredients and is believed to contribute towards reduced side effects, improved stability, increased elegance and enhanced formulation flexibility. In addition, numerous studies have confirmed that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic.

Microsponges should be uniform and spherical having the cross linked polymeric system, noncollapsible structure consisting of porous void space for the large entrapment of various active ingredients in the spaces and it should offer higher shear strength. These should be non irritant, non mutagenic, non toxic and non greasy. It should be stable at high temperature, and high shear. It should shows improved stability. It should show extended release up to 12 h.

Microsponges are microscopic spheres capable of absorbing skin secretions, therefore reducing oiliness and shine from the skin. Spherical particles composed of clusters of even tinier spheres are capable of holding four times their weight in skin secretions. Microsponge particles are extremely small, inert, indestructible spheres that do not pass through the skin. The microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis. Potentially, the microsponge system can significantly reduce the irritation of effective drugs without reducing their efficacy. The empty spheres are then washed away with the next cleansing.

Microsponges characteristic feature is the capacity to absorb or "load" a high degree of active materials into the particle and on to its surface. Its large capacity for entrapment of actives, up to three times its weight, differentiates microsponge products from other types of dermatological delivery systems.

**2. Materials and Methods:**

**2.1 Experimental design:**

Box-Behnken statistical screening design was used to statistically optimise the formulation parameters and evaluate main effects, interaction effects and quadratic effects of the formulation ingredients on the MDF of mucoadhesive polyherbal gel formulations. Response surface methodologies, such as the Box-Behnken and Central Composite Design (CCD), model possible curvature in the response function. A 3-factor, 3-level design used is suitable for exploring quadratic response surfaces and constructing second order polynomial models with Design Expert (Version 7.0.0, Stat-Ease Inc., Minneapolis, MN). The Box-Behnken design was specifically selected since it requires fewer runs than a CCD in cases of three or four variables. This cubic design is characterised by set of points lying at the midpoint of each edge of a multidimensional cube and center point replicates (n = 3) whereas the 'missing corners' help the experimenter to avoid the combined factor extremes. This property prevents a potential loss of data in those cases . A design matrix comprising of 15 experimental runs was constructed. The non-linear computer-generated quadratic model is given as Y ¼ b0 þ b1X1 þ b2X2 þ b3X3 þ b12X1X2 þ b13X1X3 þ b23X2X3 þ b11X2 1 þ b22X2 2 þ b33X2 3 ð1Þ where Y is the measured response associated with each factor level combination; b0 is an intercept; b1 to b33 are regression coefficients computed from the observed experi mental values of Y; and X1, X2 and X3 are the coded levels of independent variables. The terms X1X2 and X2 i (i = 1, 2 or 3) represent the interaction and quadratic terms, respectively. The dependent and independent variables selected are shown in Table 1 along with their low, medium and high levels, which were selected based on the results from preliminary experimentation.

**2.2 Materials:**

ORZ was donated by Licon Pharmaceutical Ltd. Pvt., Ahmedabad, Gujarat (India) Ethyl cellulose by chem dye corporation Rajkot, Gujarat (India) Methanol AR grade Merck Parikh Chem, Bharuch, Gujarat (India), Carbopol 940 SDFCL mumbai , Gujarat (India). Triethanolamine, Trishul, Bilimora Gujarat (India)

**2.3. Optimization of quasi emulsion solvent diffusion method[20-32]**

Preparation of gels Carbopol 940 (Cp-940) gels were prepared by dispersing the polymer powder in small aliquots into stirred mixtures of neutralising agent and water. After continuous stirring at 500,1000,1500 rpm for different time, the gel samples were left to hydrate completely and then centrifuged different rpm for different min to remove the air bubbles.

The pH values were determined using digital pH meter (Mettler Instruments, Germany) with glass micro-electrode. The weight ratio between the polymer and the triethanolamine used was 1:1.6

The preparation methods of microsponges are limited in the means of complexity and cost. The suspension polymerization is the known process to prepare the commercially available microsponges. Therefore, Quasi-emulsion solvent diffusion method serves an alternative way for preparing microsponges. The microsponges containing ORZ were fabricated by quasi-emulsion solvent diffusion method using an inner phase comprising Ethyl cellulose and PVA. More over ORZ was put in and dissolved through ultrasonication at 35°C. This mixture was then poured into an aqueous solution of PVA (outer phase) with stirring rate 500 rpm for 60 min. Further more, microsponges were formed due to the removal of dichloromethane and ethanol from the system by evaporation. Prepared microsponges were then filtered, washed with distilled water and subjected to drying for 12 h in hot air oven. So the final stage, microsponges were weighed to determine production yield. Various formulation batches are prepared as per table.

**Table 1.1** : Formulations of Box Behnken batches of microsponges

| Run | Independent Variable | | | Actual Value | | |
|---|---|---|---|---|---|---|
| | A | B | C | A | B | C |
| F1 | 0 | 0 | 0 | 0.5 | 1000 | 900 |
| F2 | 1 | 0 | -1 | 0.75 | 1000 | 800 |
| F3 | -1 | -1 | 0 | 0.25 | 500 | 900 |
| F4 | 0 | 1 | 1 | 0.5 | 1500 | 1000 |
| F5 | -1 | 1 | 0 | 0.25 | 1500 | 900 |
| F6 | 1 | 0 | 1 | 0.75 | 1000 | 1000 |
| F7 | -1 | 0 | -1 | 0.25 | 1000 | 800 |
| F8 | 0 | -1 | 1 | 0.5 | 500 | 1000 |
| F9 | 0 | 0 | 0 | 0.5 | 1000 | 900 |
| F10 | -1 | 0 | 1 | 0.25 | 1000 | 1000 |
| F11 | 0 | 1 | -1 | 0.5 | 1500 | 800 |
| F12 | 0 | -1 | -1 | 0.5 | 500 | 800 |
| F13 | 1 | 1 | 0 | 0.75 | 1500 | 900 |
| F14 | 0 | 0 | 0 | 0.5 | 1000 | 900 |
| F15 | 1 | -1 | 0 | 0.75 | 500 | 900 |

## 3. EVALUATION PARAMETERS:

### 3.1 Preformulation study[1-11]

The microsponge delivery system fulfills these requirements and has resulted in a new generation of very well-tolerated and highly efficacious, novel products. These products are typically presented to the consumer in conventional forms like creams, gels or lotions and they contain a relatively high concentration of active ingredients.

The overall objective of preformulation testing is to generate information useful to the formulator for mass-produced. Preformulation testing is defined as investigation of physical and chemical properties of a drug alone and when combined with excipients. This is the first step in for development of dosage forms of drug substance. Preformulation investigations are designed to identify those physicochemical properties and excipients that may influence the formulation design, method, pharmacokinetic and other properties of the resulting product.

### 3.2 Organoleptic property [10-12]

This includes recording of state, Taste, odour and colour of the drug using descriptive terminology. Record of colour of early batches is very useful in establishing appropriate specifications for later production. Drugs generally have a characteristic odour and taste. Unpleasant ones are masked later during formulation.

**3.3 Melting point determination [14,18]**
The melting point of Ornidazole was determined using melting point apparatus. The small amount of drug was placed in capillary which was placed in melting point apparatus and the temperature at which the sample is start to melt was note down. Value was compared with the reported value. This was performed in triplicates and average value was noted

**3.4 Particle size determination[12-15]**
Particle size analysis of loaded and unloaded microsponges will be performed by scanning electron microscopy. The values will be expressed for all formulations as mean size range. Cumulative percentage drug release from nanosponges of different particle size will be plotted against time to study effect of particle size on drug release.

**3.5 Determination of loading efficiency and production yield**
The loading efficiency (%) of the nanosponges will be calculated according to the following equation:

Loading efficiency = Actual Drug Content in Nanosponges X 100…….. (1)
Theoretical Drug Content

The production yield of the nanoparticles will be determined by calculating accurately the initial weight of the raw materials and the last weight of the nanosponge obtained.

Production Yield= Practical mass of nanosponges X 100…… (2)

Theoritical mass (Polymer+drug)

**3.6 SEM[3-5]**
This very useful for surface study. It is very helpful for size and shape of microsponge check.

**3.7 Viscosity measurement**
For determination of GI, Brookfield Rheometer was used in which the test material is placed between two surfaces, one surface is rotated, and the torque resisting flow is measured. This allows the determination of relationship between applied shear rate and shear stress experienced by the test material. All the measurements were conducted using spindle about 4 ml sample volume. The tests were performed in triplicate, with a coefficient of variation of less than 5% being found.Viscosity of different formulations was determined using Brookfield viscometer at temperature 37±0.5°C.

**3.8 Determination of pH**
The pH of the MPGs was recorded with a glass microelectrode (Mettler Instruments, Germany), by bringing it in contact with the MPGs and allowing it to equilibrate for 1 min. Experiments were performed in triplicate to check for the neutralisation of gels. The gels were also diluted with VFS in 1:1 ratio and the pH recorded. pH evaluation was carried out for all 15 experimental formulations and the optimised formulations prepared with three different Carbopol grades.The pH of optimized microsponge loaded hydrogel was determined using digital pHmeter. microsponge loaded gel was weighed accurately and dispersed in
of purified water. The measurement of pH of each formulation was done in triplicate and mean values were calculated.

**3.9 Diffusion[1-5]**
It is important to check control realease of drug Franz Diffusion cell is used for invitro drug release check. Perticular time interval sample is taken and take absorbance.

Stability studies Stability study of the optimised MPGs was carried out as per ICH guidelines at 25℃±2 ℃/60% ± 5% RH and 40℃±2℃/75% ± 5% RH. Physicochemical and rheological characterisation of the mucoadhesive gels was carried out over a period of 6 months at different time intervals of 1, 3 and 6 months

**4: RESULT:**
**4.1 Preformulation study:**
**1) Pure Drug characteristics:** The prepared gels were white in color . The pH of all the gel formulations prepared as per Box-Behnken design and optimized formulations were found in the range of vaginal pH range. after neutralization with triethanolamine. This characteristic compares with IP characteristic of drug and confirm that this is the same drug.

**Table 4.1 :** Pure Drug Characteristics

| **Properties** | **Results** |
|---|---|
| **State** | solid |
| **Description** | White powder |

**2) DSC:**

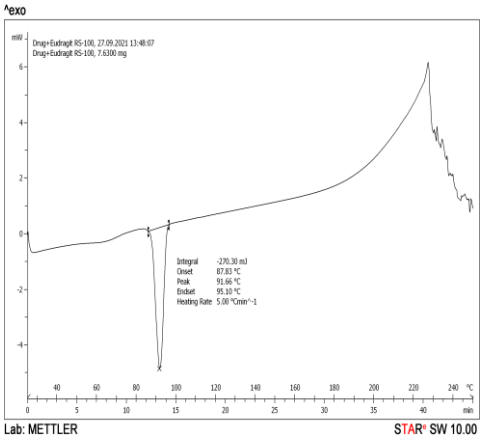



**Fig 4.1 Drug+Eudragit RS-100**

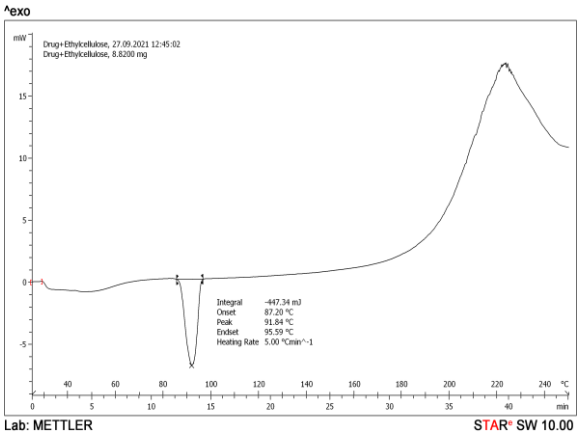



**Fig 4.2 Drug+Ethylecellulose**

**3) FTIR:**

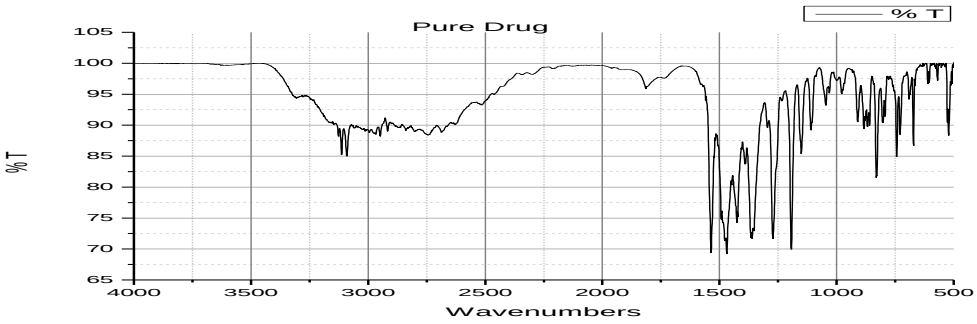



**Fig 4.3 Pure Drug**

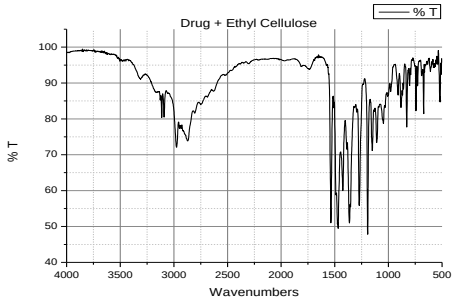



**Fig4.4: Drug and excipient of microsponge**

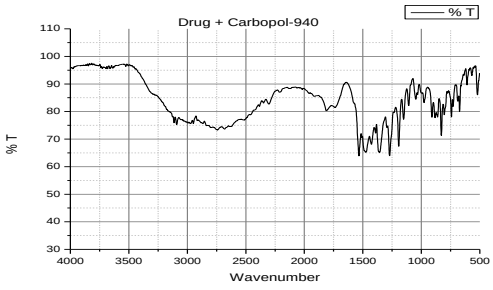



**Fig 4.5:Drug and excipient of gel**

It is important that Drug and excipient and it indicate that there is no interaction occur.

4**) x-ray of Ornidazole:**

This data show that drug is not in crystalline in nature so that useful for microsponge preparation

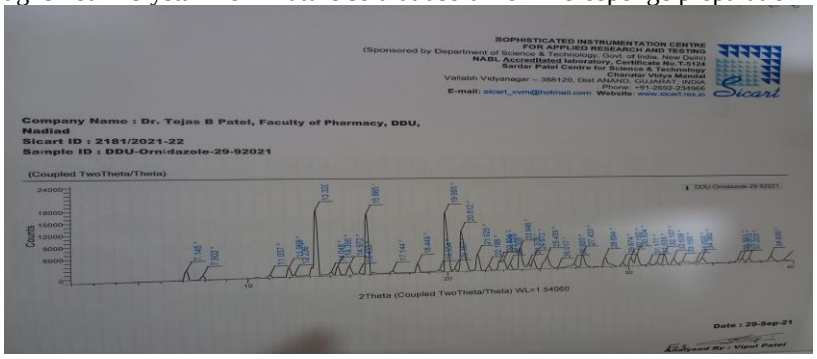



**Fig 4.6: X-Ray study of Drug**

**4.2 Organoleptic property:**
Following characteristics important for study of various type of route of drug delivery.

**Table 4.2 :** Organoleptic Property

| | |
|---|---|
| **Taste** | Tasteless |
| **Odour** | Odourless |
| **Colour** | Colourless |

**4.3 Melting point determination:**
This Pure drug melting point is very important for determination of drug degradation and preparation of various type of bulk dosage form.

**Table 4.3 :** Melting point determination

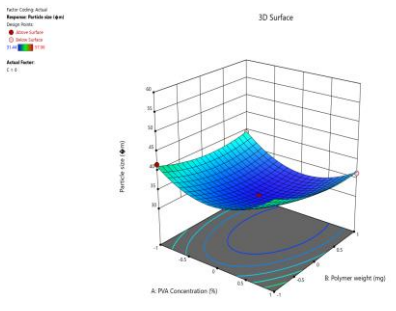
| **Experiment** | **Observation** |
|---|---|
| Melting Point Range | 85-90°C |

**4.4 Particle size determination:**
Particle size of microsponge depend on stirring speed and also stirring time. It is important for its physical appearance.

**Table 4.4 :** Particle size (*Mean ± SD; n=3 )

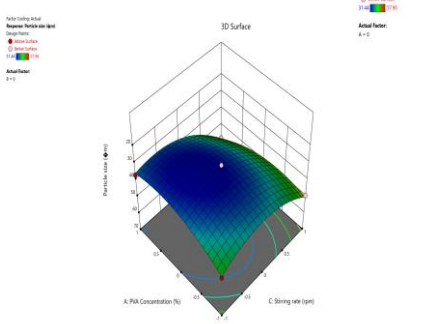
| **Batch** | **Independependent Variables** | | | **Dependependent Variables** |
|---|---|---|---|---|
| | **A** | **B** | **C** | **Y1** |
| F1 | 0 | 0 | 0 | 31.44±0.816 |
| F2 | 1 | 0 | -1 | 36.88±0.523 |
| F3 | -1 | -1 | 0 | 41.67±0.129 |
| F4 | 0 | 1 | 1 | 45.12±0.254 |
| F5 | -1 | 1 | 0 | 39.26±0.651 |
| F6 | 1 | 0 | 1 | 57.96±0.312 |
| F7 | -1 | 0 | -1 | 46.43±0.421 |
| F8 | 0 | -1 | 1 | 57.09±0.719 |
| F9 | 0 | 0 | 0 | 31.56±0.325 |
| F10 | -1 | 0 | 1 | 49.23±0.110 |
| F11 | 0 | 1 | -1 | 38.67±0.251 |
| F12 | 0 | -1 | -1 | 33.24±0.723 |
| F13 | 1 | 1 | 0 | 36.39±0.275 |
| F14 | 0 | 0 | 0 | 31.74±0.163 |
| F15 | 1 | -1 | 0 | 43.07±0.324 |

**PARTICLE SIZE : Response surface methodology**



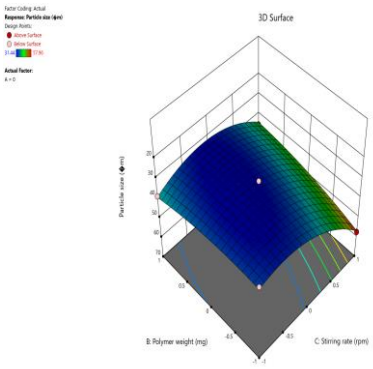

X

(Effect Of Factor A And B On Particle Size)




y

(Effect of Factor A and c on Particle size)




z

(Effect of Factor B and c on Particle size)

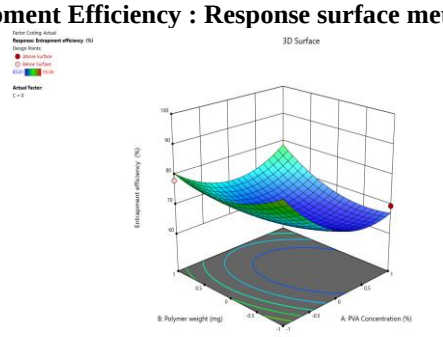
**4.5 Determination of loading efficiency and production yield:**

The determination of Entrapment efficiency and production yield is very much important. Both characters are important and depend on stirring time and stirring rate

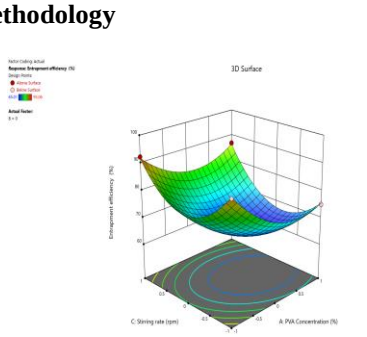
**Table 4.5** : Loading efficiency and production yield (*Mean ± SD; n=3 )

| Batch | Independependent Variables | | | Dependependent Variables | |
|---|---|---|---|---|---|
| | **A** | **B** | **C** | **$Y_2$** | **$Y_3$** |
| F1 | 0 | 0 | 0 | 65.17±0.231 | 74.51±0.831 |
| F2 | 1 | 0 | -1 | 75.02±0.365 | 66.01±0.932 |
| F3 | -1 | -1 | 0 | 88.12±0.545 | 89.54±0.254 |
| F4 | 0 | 1 | 1 | 95.06±0.167 | 93.02±0.764 |
| F5 | -1 | 1 | 0 | 78.12±0.354 | 69.16±0.831 |
| F6 | 1 | 0 | 1 | 86.92±0.838 | 85.89±0.653 |
| F7 | -1 | 0 | -1 | 90.32±0.234 | 89.82±0.264 |
| F8 | 0 | -1 | 1 | 76.58±0.163 | 86.16±0.931 |
| F9 | 0 | 0 | 0 | 65.32±0.432 | 74.17±0.853 |
| F10 | -1 | 0 | 1 | 92.34±0.162 | 91.56±0.192 |
| F11 | 0 | 1 | -1 | 79.54±0.531 | 80.97±0.179 |
| F12 | 0 | -1 | -1 | 81.93±0.753 | 79.95±0.853 |
| F13 | 1 | 1 | 0 | 76.35±0.862 | 76.35±0.621 |
| F14 | 0 | 0 | 0 | 65.01±0.531 | 74.04±0.326 |
| F15 | 1 | -1 | 0 | 69.56±0.172 | 60.08±0.539 |

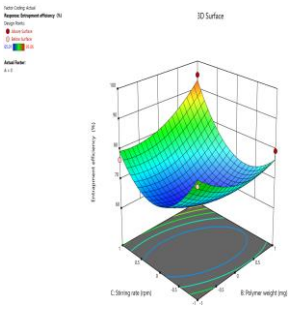
**Entrapment Efficiency : Response surface methodology**




(Effect of Factor A and B on Entrapment Efficiency )



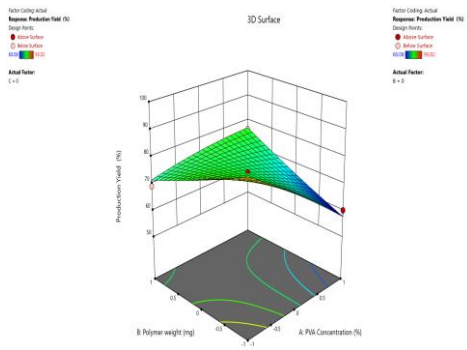

(Effect of Factor A and c on Entrapment Efficiency )




(Effect of Factor B and c on Entrapment Efficiency)

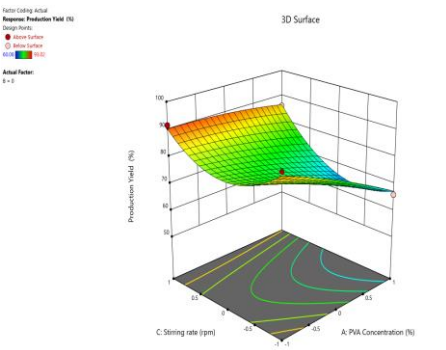
**Production yield : Response surface methodology**

X



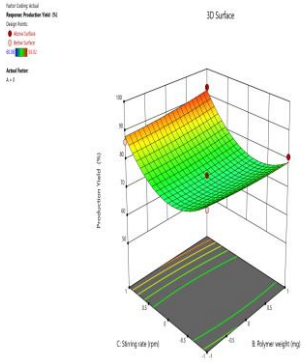

Effect of X
(Factor A and B on Production Yield)

y




Effect of y
(Factor A and c on Production Yield)

z




Effect of z
(Factor B and c on Production Yield)

**4.6 SEM:**
A scanning electron microscope (SEM) is a type of electron microscope which is useful for produces images of a sample by scanning the surface with a focused beam of light on particles. So that perfect image is generated.

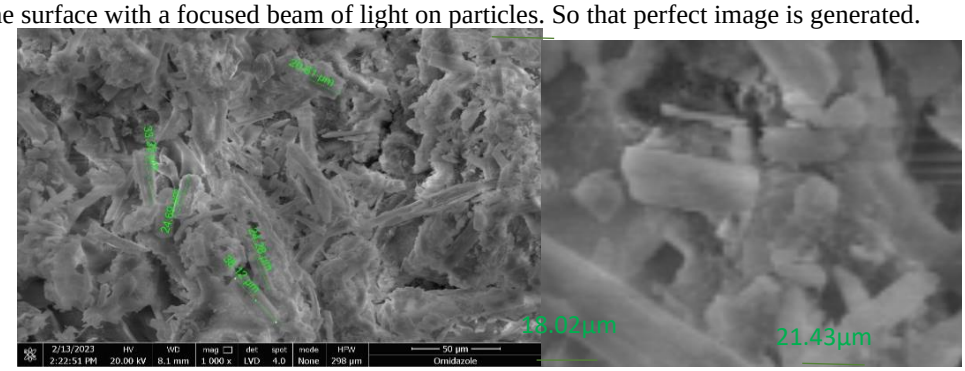



**Fig 4.7:** SEM study of ornidazole microsponge

**4.7 Viscosity measurement:** It is important characteristic for gel. For vaginal drug delivery viscous material required to adhere the vaginal skin longer period of time.

**Table 4.6:** Viscosity measurement (*Mean ± SD; n=3 )

| **Polymer** | **Weight (g)** | **Viscosity (ps)*** |
|---|---|---|
| Carbopol 940 | 1 | 1000±0.264 |
| Carbopol 940 | 1.5 | 1000±0.565 |
| Carbopol 940 | 2 | 1100±0.142 |

**4.8 Determination of pH:**
Its important for particular site. Drug delivery is effective it is nearer or same pH of the site of action. Particularly topical preparation pH is very much affective.

**Table 4.7:** pH measurement (*Mean ± SD; n=3 )

| **Polymer** | **Weight (g)** | pH* |
|---|---|---|
| Carbopol 940 | 1 | 6.81±0.005 |
| Carbopol 940 | 1.5 | 6.83±0.004 |
| Carbopol 940 | 2 | 6.87±0.003 |

**4.9 Spreadability Study:** The optimum formulation was selected based on the criteria of attaining the good value of spreadability based on this gel selected.

**Table 4.8:** Spreadability study (*Mean ± SD; n=3 )

| **Polymer** | **Weight (g)** | **Spreadability (g.cm/sec)*** |
|---|---|---|
| Carbopol 940 | 1 | 11.35±0.057 |
| Carbopol 940 | 1.5 | 12.08±0.080 |
| Carbopol 940 | 2 | 12.94±0.065 |

**4.9 Diffusion:**
Diffusion study compare with marketed Formulation (In-Vitro) (*Mean ± SD; n=3 )

**Table 4.9:** Diffusion study (*Mean ± SD; n=3 )

| **Sr. No.** | **Time (hr)** | **Pure drug** | **Marketed Gel** | **F5 formulation gel** |
|---|---|---|---|---|
| 1 | 0 | 0.00 | 0.00 | 0.00 |
| 2 | 0.5 | 2.70±0.06 | 1.60±0.06 | 0.66±0.02 |
| 3 | 1 | 6.73±0.12 | 3.87±0.14 | 3.40±0.10 |
| 4 | 2 | 13.93±0.15 | 7.97±0.58 | 9.97±0.21 |
| 5 | 4 | 16.43±0.21 | 10.22±0.41 | 12.07±0.06 |
| 6 | 6 | 19.60±0.15 | 12.80±0.78 | 13.13±0.06 |
| 7 | 12 | 22.77±0.18 | 17.38±0.59 | 18.13±0.06 |
| 8 | 24 | 25.83±0.15 | 24.92±0.84 | 20.13±0.06 |
| Jss (ug/cm$^2$/h) | | 0.67±0.07 | 0.65±0.079 | 0.52±0.07 |

| | | | |
|---|---|---|---|
| Kp (cm/h)×$10^5$ | 0.34±0.04 | 0.33±0.04 | 0.26±0.04 |

All microsponge batch provide controlled release after 12 hr. So this very important formulation for control drug delivery. Optimized batch provide higher control release this is because of PVA concentration and polymer concentration difference as well as stirring speed.

**5. DISCUSSION:**

This result presents new approaches shows that the formulation particle size very micron size in range and provide good spherical shape. The % Encapsulation efficiency is very good with high production yield. So ultimately all most of characteristics of microsponge good enough for control release formulation. The gel characteristics check all are provide good characteristics like spread ability, pH and viscosity also diffusion is control release. All above data of result confirm that gel is good for vaginal delivery and provide control release

**CONCLUSION:**

Mucoadhesive vaginal gels of using Carbopol 940 were prepared and optimized using Box-Behnken design. The quantitative effect of these factors at different levels on the maximum detachment force could be predicted by using polynomial equations. Linearity observed between the actual and predicted values of the response variables. The optimized formulation was prepared and the relationship between oscillatory rheology and mucoadhesive performance of the gels was studied. Stability study of the optimized formulation proved the integrity of the developed gels. This study presents new approaches for the modification of gel as novel delivery as well as a new system with a great potential for vaginal drug delivery. The unique compressibility of microsponges offers a new alternative way for producing porous structure and provide control drug delivery. The vaginal drug delivery provides formulations with proper drug required pH and good compatibility of patient. The microsponges vaginal drug delivery were prepared based on two approaches. Both two approaches, using the triggering vaginal microorganism. The microsponge formulated successfully and provide good characteristics for vaginal drug delivery. The optimized formulation has good characteristics like particle size, loading efficiency and encapsulation efficiency. This type of formulation provides control drug delivery and decrease application time.

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