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# Formulation and Evaluation of Nanosponge Hydrogel for Transdermal Release of Curcumin

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## ABSTRACT

Curcumin is a hydrophobic component that shows anti-cancer, antioxidant properties but it faces problem for its bioavailabilty .To overcome this problem Curcumin is encapsulated into a nanosized polymeric structure called as nanosponge.This polymeric encapsulation provides sustained and control release of curcumin from its hydrogel matrix. Encapsulation was done with the help of various concentration of Ethyl cellulose as a polymeric matrix and Polyvinyl Alcohol as a stabilizer.

A $3^2$ factorial design was employed to investigate effect of EC:HPMC K100 and PVA on drug entrapment efficiency,drug release .Resuls indicated that wehe we reduce the concentration of Ethyl cellulose Drug entrapment efficiency decreases and drug release increases.So,it highlights balance between polymer concentration and Drug release.

Then the optimized nanosponge formulation was incorporated in a hydrogel matrix by varying concentration of Carbopol 940 and investigating its effect on spreadability,viscosity and permeation.So we can tailor the drug release and spreadibility of the hydrogel matrix by changing the concentration of Carbopol.

So the study reveals that careful modification of the formulation factors significantly affect the transdernal release of curcumin loaded nanosponge hydrogel.This system gives a promising approach of controlled and sustained release of curcumin in breast cancer through a non-invasive strategy and less side effects.

***Keywords:*** *Curcumin, Anticancer, Nanosponges, Hydrogel, Ethyl cellulose, Hpmc K100,Quasi Emulsion Diffusion method, Breast Cancer, Transdermal release.*

## 1. INTRODUCTION

Regardless of lot of efforts still dangerous human diseases like Cardiovascular diseases, cancer, and neurological diseases etc have not decreased till now. Scientists have discovered numerous smart drugs which target on specific signaling pathways that cause a sudden change in the body and trigger a disease. But considering above points smart drugs are often costly and have numerous side effects. So there is a need of medications that is of low cost, can target various signaling pathways, should have fewer problematic consequences,should be easily available in the daily life routine for avoiding and treating various human diseases[(1)(2).]

Curcumin is a polypotent or multiactioned molecule that can interact at various target site[(3).]It is a neutraceutical that is a polyphenol which possess antioxidant, anticancer, anti-inflammatory, anti-microbial, and wound healing properties[(4).] It's a traditional drug that has been used from decades for prevention and treatment of various diseases. Numerous preclinical studies have been conducted on Curcumin for past three decades[(5).]Curcumin is derived from a rhizome called *Curcuma Longa*[(6).]Curcumin is a lipophilic molecule and can pass through the cell membrane easily .It is used as spices and as a natural food coluring agent[(7).]Important molecules for curcumin binding include transcription factors, inflammatory mediators, and enzymes such as histone acetyltransferase, reductase and protein kinase. Curcumin is a potent epigenetic regulator in various

disease like cancer. Additionally by inhibiting the phosphorylase kinase enzyme it can modify number of proteasomal pathways [8].

Curcumin in Breast Cancer:In breast cancer there is over activation of nuclear factor kappa B which is responsible for survival, proliferationand metastasis of cancerous cell. Curcumin inhibits nuclear factor κBp65 factor which is a key factor for NF –Kbpathway. This reduces breast cancer ability to move, migrate, grow and invade to other tissues. Another breast cancer factor is HER2 protein which promote tumour growth. Curcumin reduces HER2 protein levels and reduces activation and phosphorylation of key growth pathways like AKT and MAPK and it also reduces RON mediated invasion.[9][10][11]

Curcumin has poor aqueous solubility and low bioavailability. Its poor bioavailability is due to its fast metabolism, poor absorption and fast elimination. To overcome this problem there are various promising approaches like, nanoparticles, liposomes, micelles, nanosponges, microsponges and phospholipid complexes .[12-14]

To overcome this problem Nanosponges act as best carrier as they can efficiently solubilize poorly water soluble drugs and can give a prolonged drug release. Nanosponges can be beneficial for both hydrophobic and hydrophilic drugs because of their internal hydrophobic cavities and external hydrophilic nature [15].

Nanosponges are prepared by various methods namely Hypercrosslinked β Cyclodextrin method, Emulsion Solvent Diffusion method, Quasi emulsion method, Ultrasound Assisted synthesis, etc. Nnaosponge is a drug carrier that uses polymers to entrap the drug which reduce its degradation and provide a sustain and controlled drug release at the site of action[18]

The most widely used technique for creating nanosponges is the quasi emulsion solvent diffusion method, which allows for dissolving a water- insoluble polymer in an organic solvent and then making it solubilize in an aqueous phase with a surfactant which is hydrophillic. The organic solvent is then removed by constant stirring and leaving behind spherical particles. The spheres are formed by polymer with internal and external pores[16].There are factors that affect pore formulation polymer ratio, organic spolvent, emulsifier concentration, stirring rate.[17]

We have developed a formulation of nanosponges by using ethyl cellulose and hydroxypropyl methylcellulose as polymers loaded with the selected drug curcumin.Here we have changed the concentration of ethylcellulose and observed the drug entrapment efficiency of the nanosponges. Additionally the influence of polyvinyl alcohol with various concentration which is used as an emulsifier was observed.

## 2. MATERIALS AND PROCEDURES

### 2.1 Materials

.Curcumin was purchased from LOBA chemie pvt ltd, Mumbai,Hpmc K100 and Dichloromethane was purchased from Solanki Excipients,Pune, Ethyl Cellulose ,Polyvinyl alcohol, Carbopol 940,Triethanolamine,Methyl Paraben, Propylene glycol was used from the research lab of the intstitute.

### 2.2 Method of Preparation for Curcumin Nanosponges [19]

Nanosponges were formulated by quasi emulsion diffusion method

**Preparation of Internal phase**:Varying ratio of Ethylcellulose(EC),Hpmc K100 and Curcumin were dissolved in 20 ml of Dichloromethane(DCM).This solution forms the polymeric organic phase(Internal Phase)

**Preparation of External Phase**:Different concentration of Polyvinyl alcohol (PVA) were dissolved in 100 ml of Distilled water.This formed the aqueous (external phase),acting as emulsifying medium.

**Emulsification**:Under continuous stirring the internal phase was gradually introduced to the external phase,stirring was done under high speed homogeniser at 5000 rpm.

**Solvent Diffusion and Evaporation**:Stirring was continued for 4 hours at room temperature to allow evaporation of DCM,leading to formation of nanosponges.

**Filtration and washing**:The formed Nanosponges were filtered using whatman cellulose filter paper.They were washed with double distilled water to remove excess PVA and other residues.

**Drying**:The nanosponges were dried at 40°C for 24 hours to ensure removal of residual solvents.

**Factorial batches with $3^2$ factorial design**

**Table no 2.1: Variables in $3^2$ factorial design**

| Independent Variables | Levels used | | |
|---|---|---|---|
| | -1 | 0 | +1 |
| X1=Polymer ratio(Ethyl Cellulose:Hpmc K100) | 7:1 | 8:1 | 9:1 |
| X2=Concentration of polyvinyl alcohol | 0.1 | 0.25 | 0.5 |

**Response Variables:**

Y1=Percentage yield, Y2=Entrapment Efficiency

**Table no 2.2 Experimental Runs for $3^2$ Factorial Design**

| No of Runs | Drug (CUR) mg | EC:HPMC | PVA% | WATER (Ml) | DCM (Ml) |
|---|---|---|---|---|---|
| F1 | 250 | 9.1 | 0.1 | 100 | 20 |
| F2 | 250 | 9.1 | 0.25 | 100 | 20 |
| F3 | 250 | 9.1 | 0.5 | 100 | 20 |
| F4 | 250 | 8.1 | 0.1 | 100 | 20 |
| F5 | 250 | 8.1 | 0.25 | 100 | 20 |
| F6 | 250 | 8.1 | 0.5 | 100 | 20 |
| F7 | 250 | 7.1 | 0.1 | 100 | 20 |
| F8 | 250 | 7.1 | 0.25 | 100 | 20 |
| F9 | 250 | 7.1 | 0.5 | 100 | 20 |

**2.3 Characterization of Curcumin loaded Nanosponges(Cur-Ns)**

**1. Visual Appearance:**The nanosponges were observed for their colour and shape

**2. Theoretical Yield:**Theoreotical yield =Actual amount of drug added + Actual amount of polymer added

**3. Practical Yield:**Determination of dried nanosponges recovered from the batches

**4. Percentage Yield [46][47][48]:**The weight of dried nanosponges(W1) recovered from batches and the total of the original dry weight of beginning material (W2) were used to compute the production yield percentage(wt/wt) using the formula below

% Production yield = W1/W2 × 100

**5. Particle size analysis**

Determination of the average particle size of nanosponges was carried out by Horiba Scientific SZ-100 For the determination of particle size the prepared formulations were suitably diluted with 2 ml of ethanol and diluted upto 10 ml with distilled water. The Horiba Scientific SZ100 was used to determine the particle size of the nanosponge after the dilution.

**6. Analysis of Zeta Potential [23]**

The Light scattering method was used to determine the prepared nanosponges Zeta potential. The sample must be completely transparent in order to determine the zeta potential. When the solution is prepared for analysis, it should be carefully into the cuvette to prevent bubbles from formin on the cuvette walls. It might also be possible to get rid of the bubbles by gently titling the cuvette or tapping it on a hard surface. After that the electrode was dipped within the sample solution containing cuvette. Bubbles in between the electrodes should be avoided. It is possible to insert the solution containing cuvette into the device. Zeta potential. Analysis was performed using the same tool that was utilised for particle size analysis.

**7. Index of Polydispersity**

Using the Dynamic light scattering(DLS),the produced nanosponges was calculated for its Polydispersity index(PI) .The sample must be crystal clear to very slightly hazy for the DLS technique to work. If the mixture is excessively white it should be further diluted before perfomin DLS size assessment because it is cloudy. When the solution is prepared for analysis, it should be carefully transferred into the cuvette to prevent bubbles from forming on the surface of the cuvette. The cuvette holding the solution can be inserted into the device once it is homogeneous and prepared for DLS measurement.

**8. Entapment Efficiency** [20] [21][22]

Entrapment efficiency = Actual drug loading / Theoretical drug loading × 100

**9. In Vitro drug release study** [24]

A six-vessel USP class II dissolution apparatus (Curio 2020+paddle apparatus) was used to assess the invitro drug dissolution from nanosponges. With paddle rotation set at 50rpm,a 10 mg drug equivalent sample of nanosponges was kept at 37± 0.5 °C in 500 ml of phosphate buffer (pH 7.4).For total of 24 hrs ,a 5 ml of sample was taken at prearranged intervals. After every sampling the dissolving media was refilled with freshly prepared phosphate buffer to preserve the sink condition. A uv visible spectrophotometer set to 425 nm was used to analyse the samples in triplicate, and the % drug release was computed using a number of standard solutions

**10. Scanning electron Microscopy or surface morphology**

Particle size distribution, surface topography, roughness, and the morphology of the sectioned surface have all been determined using scanning electron microscopy. Due to its ease of use and simplicity in sample preparation, SEM is most likely the most widely used technique for characterising drug delivery system. SEM experiments were conducted in Infinite Biotech, Sangli.

**11. DSC (Differential Scanning Colorimetry)**

Mettler Toledo(*SW920) Differential Scanning Colorimeter using aluminium pan equipped with an intercooler and a refrigerated cooling system was used to analyze the thermal behaviour of Curcumin which shows an endothermic peak at 184°C

**2.4 Formulation of hydrogel of optimized batch of Curcumin Nanosponge**[25]

A precisely weighed amount of Carbopol 940 was dispersed in approximately 20 ml of distilled water and allowed to hydrate for 24 hours. After complete soaking, the dispersion was neutralized using triethanolamine (TEA) under continuous stirring to facilitate gel formulation .

In another container, the required quantity of methyl paraben and the drug-loaded nanostructure(NS)-equivalent to the desired topical dose ,were dissolved in propylene glycol with gentle stirring to ensure homogeneity. This solution was then gradually added to the pre-neutralized Carbopol dispersion while stirring continously.

The combined mixture was subjected to further mixing for 20 minutes to achieve a uniform gel base. The resultant dispersion was then kept undisturbed for 60 minutes at room temperature to allow complete hydration and swelling of the gel components.

All prepared gel formulations were allowed to equilibrate for a minimum of 24 hrs at room temperature before proceeding with viscosity measurements and other physicochemical evaluations.

**Table 2.3.Formulation table for hydrogel**

| Formulation Code | Carbopol 940 | Propylene Glycol | Methyl Paraben | Triethnolamine |
|---|---|---|---|---|
| G1 | 0.4 | 0.5 | 0.02 | 0.1 |
| G2 | 0.5 | 0.5 | 0.02 | 0.1 |
| G3 | 0.6 | 0.5 | 0.02 | 0.1 |

**2.5 Evaluation of hydrogel.**

1] Physical inspection: The colour, homogeneity, consistency and appearance of the produced hydrogel compositions were assessed visually

2] pH:A digital pH meter was used to determine the pH values of 1% aqueous solutions of the produced gel

3] Viscosity: The brookfield –DV-II+Pro Viscometer was used to measure the viscosity of the hydrogel that were manufactured. Spindle no .7 was rotated at 0.5 rpm to test the apparent viscosity at 25°C

4] Spreadability: It was determined by wooden block and glass slide apparatus. It consists of two parallel-placed platforms to hold the glass slides. It is because of these parallel-placed platforms that the upper slide will be pulled in a straight line when force is applied. A pulley is centrally attached to the upper slide. Scale is fixed on one of the platforms to measure the time taken to move the slide a fixed distance. The pan was filled with weights weighing around 20 g and the amount of time

it took for the removal of upper slide to disengage from the fixed slides recorded.

5] Ex-vivo permeation investigation: Franz diffusion apparatus was used to conduct this experiment. The vertical type Franz diffusion cell was designed, fabricated, and validated, before diffusion study, the cello phonic membrane of approximately 2.5cm³ area was taken and these slices were hydrated in phosphate buffer (pH-7.4) overnight before use. After assembling the entire cell, 100 mg of the gel sample was put on the membranes surface which is connected to the donor compartment's bottom. The receptor's capacity was maintained at 25 ml. The way the cell was put together, the membrane was drained to the surface of the permeation fluid(phosphate buffer 7.4)was kept at 37±1°C constantly swirled using a magnetic stirrer at 50 rpm.1 ml sample was removed and observed in UV spectroscopy for drug content. Following each sampling, fresh buffer was then was then added back to replenish the fluid. For every gel formulation samples were taken at 0.5,1,2,3,4,5,6,7,8 hours at every sample the total amount of medication that has diffused out through the membrane was determined and noted(cumulative percentage of drug release)

## 3. RESULT AND DISCUSSION

### 3.1. Characterization of Curcumin Nanosponges

**Table 3.1 Depict Theoretical yield, Practical yield, Percentage yield, Entrapment Efficiency**

| Formulation Code | Theoretical Yield(gm) | Practical yield(gm) | Percentage Yield(gm) | Entrapment Efficiency (%) |
|---|---|---|---|---|
| F1 | 10.25 | 5.8 | 62.70% | 70.1±3.5 |
| F2 | 10.25 | 4.9 | 59.39% | 76.5±1.8 |
| F3 | 10.25 | 4.8 | 58.18% | 74.3±2.7 |
| F4 | 9.25 | 5.7 | 55.60% | 66.1±1.3 |
| F5 | 9.25 | 5.1 | 55.13% | 73.4±3.7 |
| F6 | 9.25 | 4.5 | 47.36% | 70.9±2.5 |
| F7 | 8.25 | 4.2 | 40.97% | 71.6±3.6 |
| F8 | 8.25 | 3.97 | 38.7% | 68.1±1.4 |
| F9 | 8.25 | 3.2 | 38.6% | 69.1±3.4 |

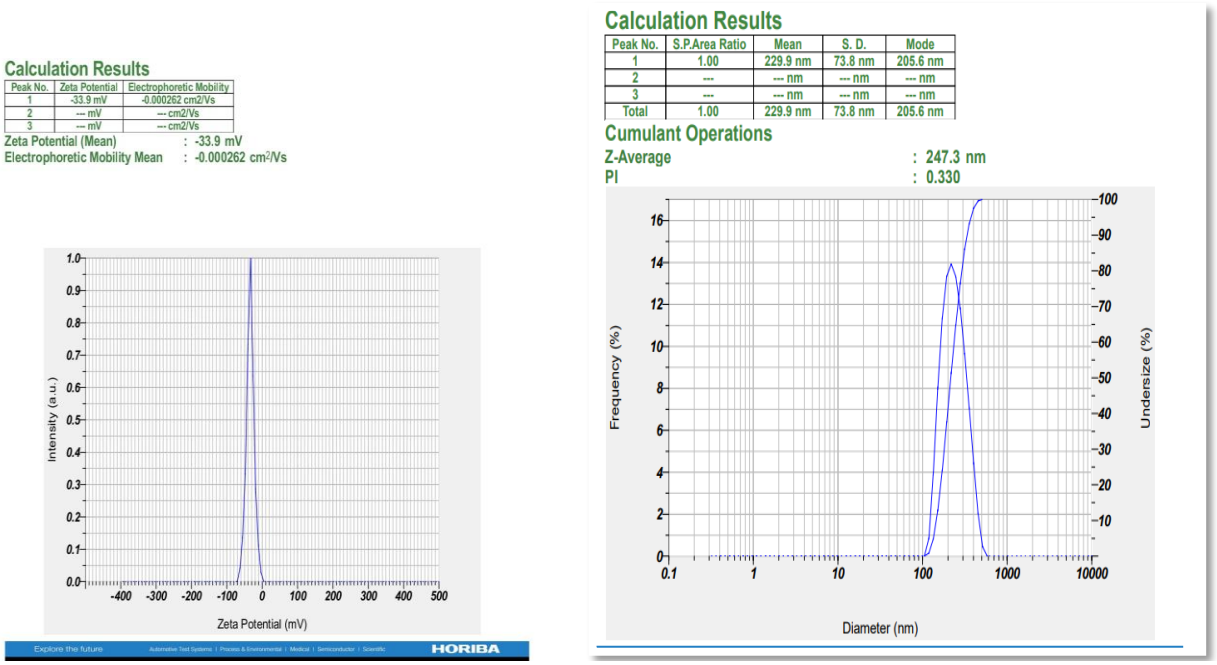


**Fig. 3.1 Particle Size, Zeta Potential,Polydispersity Index**

### 3.2 Particle Size, Zeta potential, Polydispersity index and DSC and SEM

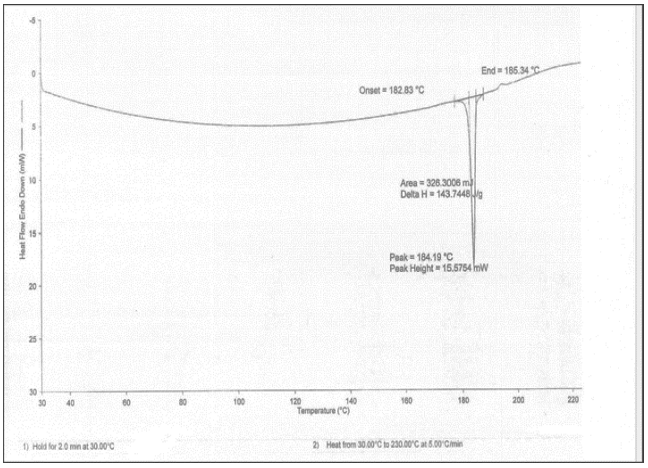


**Fig 3.2 DSC of Curcumin**

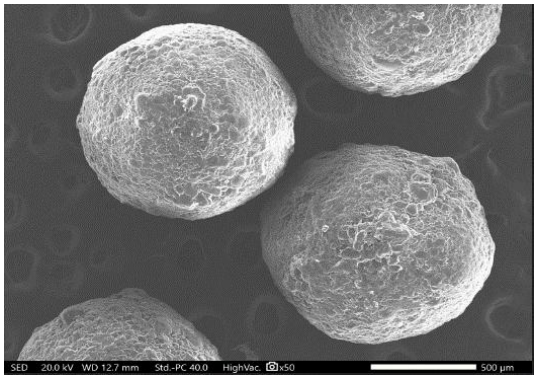


**Fig 3.3 SEM of Nanosponge**

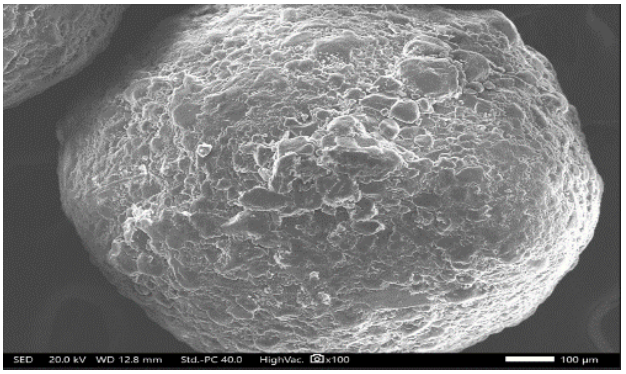


**Fig 3.4 SEM of Nanosponge**

### 3.4 In vitro drug drug release

Table 3.2 In vitro release data

| Formulation Code | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Drug Release at (24hrs) | 80±1.53 | 85±2.08 | 90±1.15 | 86±1 | 77±0.58 | 77±2.08 | 95±1.73 | 88±1.15 | 75±1.15 |

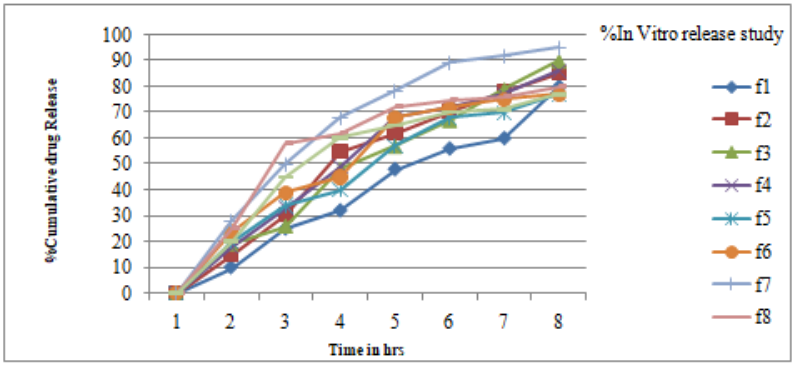


Fig 3.5 %In vitro Release study.

**3.5 Evaluation of Optimized batch of Hydrogel**

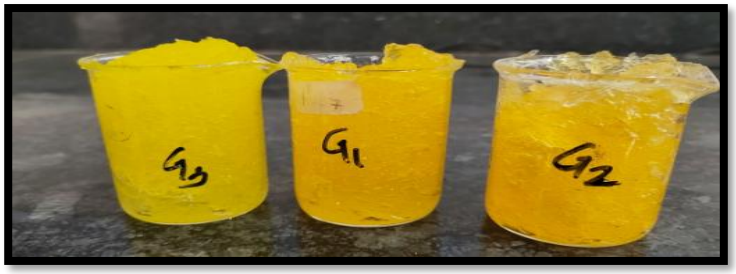


**Fig 3.6 Visualisation of Gel**

**1) Spreadability:**

**Table 3.3 Spreadability data**

| Code | Spreadability(gm/sec) |
|---|---|
| G1 | 19.2 |
| G2 | 17.5 |
| G3 | 15.8 |

**Observation-**Higher concentration of Carbopol 940 reduces spreadability

**2) pH :**(for topical application pH should be 4.5-7)

**Table 3.4 pH data**

| Code | pH |
|---|---|
| G1 | 6.3 |
| G2 | 6.4 |
| G3 | 6.6 |

**3) Viscosity**

**Table 3.5 Viscosity data**

| Code | Viscosity(cp) | Observation |
|---|---|---|
| G1 | 4000 | Smooth and good flow |
| G2 | 5200 | Moderate viscosity |
| G3 | 6200 | Thick gel |

**Observation:** G1 has low concentration of Carbopol so its depicting low viscosity, G2 has high concentration of carbopol depicting high viscosity

**4) Ex-vivo permeation study**

**Table 3.6 Ex-vivo permeation data**

| Formulation Code | G1 | G2 | G3 |
|---|---|---|---|
| Drug Permeation at (8 hr) | 90.2±3 | 84±2 | 74±1.73 |

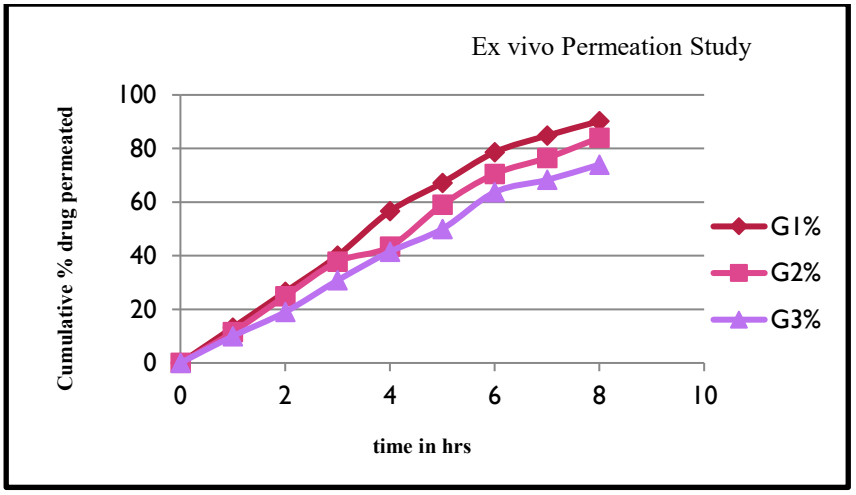


**Fig 3.7 Ex vivo permeation study**

## 4. CONCLUSION

Curcumin loaded nanosponge hydrogel was prepared successfully,this nanosized curcumin nanosponges showed that reducing the concentration of ethyl cellulose decreases entrapment efficiency and increases the drug release.Different cincentration of EC:HPMC and PVA(polyvinyl alcohol) were taken following $3^2$ factorial design for formulation of nanosponges .Hydrogel was prepared by using different concentration of Carbopol 940 and observing its effect on spreadability,viscosity and permeation.So,the present study reveals the effect of EC,HPMC K100,Carbopol 940 and PVA on preparation of overall Curcumin loaded nanosponge hydrogel for transdermal release of Curcumin for breast cancer.It highlights effect of this excipient in tailoring the physicochemical characteristics and performance of curcumin loaded nanosponge hydrogel.The factorial design approach allowed for systemic evaluation and optimization of formulatiom components.Te final product attributes for controlled and sustained transdermal release of the drug.

## REFERENCES

[1] Frantz S. Drug discovery: playing dirty. Nature. 2005 Oct 13; 437(7061).

[2] Mencher SK, Wang LG. Promiscuous drugs compared to selective drugs (promiscuity can be a virtue). BMC clinical pharmacology. 2005 Dec; 5:1-7.

[3] Mencher SK, Wang LG. Promiscuous drugs compared to selective drugs (promiscuity can be a virtue). BMC clinical pharmacology. 2005 Dec;5:1-7.

[4] Aggarwal BB, Sung B. Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets. Trends in pharmacological sciences. 2009 Feb 1;30(2):85-94

[5] Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. The international journal of biochemistry & cell biology. 2009 Jan 1;41(1):40-59.

[6] Hosseini A, Hosseinzadeh H. Antidotal or protective effects of Curcuma longa (turmeric) and its active ingredient, curcumin, against natural and chemical toxicities: A review. Biomedicine & pharmacotherapy. ss2018 Mar 1;99:411-21.

[7] Den Hartogh DJ, Gabriel A, Tsiani E. Antidiabetic properties of curcumin I: Evidence from in vitro studies. Nutrients. 2020 Jan 1;12(1):118.

[8] Giordano A, Tommonaro G. Curcumin and cancer. Nutrients. 2019 Oct 5;11(10):2376.

[9] Liu D, Chen Z. The effect of curcumin on breast cancer cells. Journal of breast cancer. 2013 Jun 28;16(2):133.

[10] Chiu TL, Su CC. Curcumin inhibits proliferation and migration by increasing the Bax to Bcl-2 ratio and decreasing NF-κBp65 expression in breast cancer MDA-MB-231 cells. International journal of molecular medicine. 2009 Apr 1;23(4):469-75.

[11] Kim HI, Huang H, Cheepala S, Huang S, Chung J. Curcumin inhibition of integrin (α6β4)-dependent breast cancer cell motility and invasion. Cancer Prevention Research. 2008 Oct 1;1(5):385-91.

[12] Tabanelli R, Brogi S, Calderone V. Improving curcumin bioavailability: Current strategies and future

perspectives. Pharmaceutics. 2021 Oct 17;13(10):1715.

[13] Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. Foods. 2017 Oct;6(10):92.

[14] Jamwal R. Bioavailable curcumin formulations: A review of pharmacokinetic studies in healthy volunteers. Journal of integrative medicine. 2018 Nov 1;16(6):367-74.

[15] Osmani AM, Hani U, R Bhosale R, K Kulkarni P, Shanmuganathan S. Nanosponge carriers-an archetype swing in cancer therapy: a comprehensive review. Current drug targets. 2017 Jan 1;18(1):108-18.

[16] Rizkalla CM, latif Aziz R, Soliman II. In vitro and in vivo evaluation of hydroxyzine hydrochloride microsponges for topical delivery. AapsPharmscitech. 2011 Jul 29;12(3):989.

[17] Cai Y, Chen Y, Hong X, Liu Z, Yuan W. Porous microsphere and its applications. International journal of nanomedicine. 2013 Mar 15:1111-20.

[18] Shivani S, Poladi KK. Nanosponges-novel emerging drug delivery system: A review. International journal of pharmaceutical sciences and research. 2015 Feb 1;6(2):529.

[19] Shahzad Y, Saeed S, Ghori MU, Mahmood T, Yousaf AM, Jamshaid M, Sheikh R, Rizvi SA. Influence of polymer ratio and surfactants on controlled drug release from cellulosic microsponges. International journal of biological macromolecules. 2018 Apr 1;109:963-70.

[20] Babaji JK, et al. formulation and evaluation of ketoconazole microsponge gel by quasi emulsion solvent diffusion. Cell Tissue Res. 2011, page no; 11(1):2691-6.

[21] Shaha Viral, et al. Microsponge drug delivery: a review. Int J Res Pharm Sci. 2010, page no;1(2):212-8.

[22] Embil K, Nacht S. The Microsponge Delivery System (MDS): A Topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. J Microencapsul. 1996;13(5), page no:575-88. doi: 10.3109/02652049609026042, PMID 8864994.

[23] Gore K, Bhattacharya S, Prajapati B. Recent Pharmaceutical Developments in the Treatment of Cancer Using Nanosponges. InAdvanced Drug Delivery Systems 2022 Jul 14.

[24] Westrin BA, Axelsson A, Zacchi G. Diffusion measurement in gels. Journal of Controlled Release. 1994 Jul 1;30(3):189-99.

[25] Iriventi P, Gupta NV, Osmani RA, Balamuralidhara V. Design & development of nanosponge loaded topical gel of curcumin and caffeine mixture for augmented treatment of psoriasis. DARU Journal of Pharmaceutical Sciences. 2020 Dec;28:489-506.