Research Article

Nanosponges loaded with 5-Fluorouracil for treatment of skin cancer

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Received: 12 May 2023 Revised: 23 July 2023 Accepted: 28 July 2023

Abstract

Background: Skin cancer is the leading type of cancer worldwide. It remains challenge to researcher to develop potent anticancer drug. 5-fluorouracil is potent anticancer drug. **Objective**: In this work we formulated 5-FU loaded nanosponge of and evaluated the formulation for the treatment of skin cancer. **Material and methods**: Formulated nanosponge pass through the skin and showed potent therapeutic effect at the application site. Six formulations of nanosponges were evaluated for entrapment efficiency, Zeta potential and SEM. **Results and Conclusion**: Formulation F4 showed better entrapment of drug, so it was further used for gel formulation. Carbopol was incorporated in nanosponge gel and prepared 4 formulations. All of these four formulations were evaluated for different parameters like pH determination, viscosity, spreadibility, drug content and in vitro drug release. Formulation G3 was contains 94% drug and drug release was found to be 92%.

Keywords: 5-Fluorouracil, skin cancer, nano sponge gel, carbopol

Introduction

Cancer is a major cause of death in universe. Skin is the largest organ of human body, which also acts as a boundary between body and environment. It protects the body from chemical, physical, and microbial injury, loss of water, and other endogenous substances. Skin cancer is fatal public health concern rising in nonstop manner in all over the world. Absorption of drug through the skin is influenced by several factors like molecular size, lipophilicity, and pH of formulation, penetrate concentration, chemical enhancers, skin hydration, skin enzymes, temperature, formulation compositions etc and are discussed briefly.

When drugs are applied on the skin surface, penetration into and through the skin can occur via various routes. Drugs penetrate either via the stratum corneum (trans epidermal) or via the appendages (trans appendageal). During penetration through the stratum corneum, two possible routes can be distinguished, (i) Penetration treating through the corneocytes and the lipid lamellae (transcellular route) and (ii) Penetration along the tortuous pathway along the lipid lamellae (intercellular route). Generally, it is accepted that the predominant route of penetration through the stratum corneum is the intercellular route. This is mainly caused by the densely cross-linked cornified envelope coating the keratinocytes. However transcellular transport for small hydrophilic molecules such as water cannot completely be excluded. The appendage route or shunt route includes either the duct of the eccrine sweat glands or the follicular duct. The content of the eccrine sweat glands is mainly hydrophilic, while the content of the follicular duct is lipophilic. This is mainly due to the sebum excreted into the opening of the follicular duct. It is generally accepted that due to its large surface area, passive skin permeation mainly occurs through intact stratum corneum (Prabhakar et al., 2013).

Fluorouracil (5-FU) is a type of chemotherapy that exerts its anti-cancer effect by preventing the production of DNA in the cell. Lack of functional DNA prevents the cancer cell from reproducing and making vital proteins, which then results in death of the cell. Topical fluorouracil is used to treat actinic keratosis and superficial basal and squamous cell skin cancers. Topical chemotherapy with 5-FU is associated with the limitations of poor skin permeation, retention at target site, and skin irritation potential.

Now a days nanoparticles of antibacterial agent are widely

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DOI: https://doi.org/10.31024/ajpp.2023.9.4.2

used, and they are highly effective and acquire huge attention as they satisfy the requirements where antibiotics fail to prevent the development of Multi-Drug Resistant mutants.

Nano-sponges have emerged as one of the maximum capable fields of existence technology due to their software in managed drug delivery. Nano-sponges are tiny sponges can travel around the body till they encounter the exact goal site and stick on the surface and begin to discharge the drug in a managed and predicted way. It is singular method for controlled drug shipping on topical application. They are non-nerve-racking, non-mutagenic, nonallergenic and innocent (Trotta and Mele, 2019). Nano-sponges are minute mesh-like systems used for curing of various illnesses and this generation is instances more treasured at turning in drugs for breast cancer than traditional techniques. Nano-sponges are nanometres molecules having big cavities, in which an extensive variety of drug may be encapsulated. These particles are able to sporting each lipophilic and hydrophilic substances and of enhancing the solubility of weakly water-soluble molecules (Vyas et al., 2008).

As compared to other nano- particles, nano-sponges are insoluble in water and organic solvents, porous, non-toxic and steady at excessive temperatures as much as 300°C. Another critical function of those nano-sponges is their aqueous solubility which permits the usage of those systems correctly for drugs with low solubility. The nano-sponges are solid in nature and may be define as oral, parenteral, topical or inhalational dosage administration. For oral administration tablets; for parenteral administration, they combined with disinfected water, salty or other aqueous solution. For topical administration, they may be effectively incorporated into hydrogel.

The researchers at Vanderbilt University and Emory University newly reported a controlled release nano-particle drug delivery machine, which can be an advanced shipping approach for turning in anticancer therapies, along with direct injection into tumour site. These nano-particles float are inside the body until they come upon the surface of a tumour cell, where they adhere to the surface and begin freeing the drug in a controlled and predictable way (Nichols and Bae, 2012).

By delivering the anti-cancer agent directly to the cancerous tissues, a nanosponge decreases the adverse effects on other tissues and increases its potency by delivering a higher concentration of the drug directly on the tumor cells. These nano-sponges are very novel and versatile and can be adapted to delivery of proteins, peptides, DNA and smaller chemical compounds like most drugs (Sanvicens and Marco, 2008). They can be synthesized to be of specific size and to release drugs overtime by varying the proportion of cross linker to polymer. The engineering capacity of nanosponge is due to the relatively simple chemistry of its polymers and cross linkers compared to many other nanoscale drug delivery systems (Selvamuthukumar et al., 2012). There are various advantages of nano-sponge: (a) Porous, nontoxic and stable at high temperatures; (b) They can be easily regenerated by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating, or changing pH or ionic strength. Due to all these characteristics, nano-sponges have been employed in different fields, such as cosmetic and pharmaceutical sectors (Alongi et al., 2011).

Based on more occurrence of skin cancer and deficiency of drug delivery system, it is necessary to make novel formulation for effective treatment of skin cancer. In the present research work we are planning to make 5-FU loaded nano-sponges based topical gel formulation for skin cancer treatment.

Materials and methods

Drug and other excipients

All the reagents and solvents used in this research work were of analytical grade and obtained from E. Merck India Ltd. Drug 5-Fu was taken from company as a sample. Electronic Weighing Balance of A and D Company HR 200 used for weighing drug and other materials. For continuous stirring of material, we used Mechanical Stirrer Remi Motors, India and Magnetic Stirrer MC Dalal & amp; Co India. Concentration of drug was found out by using Shimadzu UV Visible Spectrophotometer. Stability Chamber of Inlab Equipment Madras PVT (LTD) was used.

Preformulation studies

Preformulation studies is to develop the elegant, stable, effective, and safe dosage form by establishing kinetic rate profile, compatibility with the other ingredients and establish Physicochemical parameter of new drug substances. We also determine physicochemical properties of another excipient. Drug may be safe, stable, and effective in develop dosage for, all the excipients should be compatible with drug. This could provide important information for formulation design or support the need for molecular modification. Every drug has intrinsic chemical and physical properties which has been consider before development of pharmaceutical formulation. This property provides the framework for drugs combination with pharmaceutical ingredients in the fabrication of dosage form. Drug solubility, partition coefficient, dissolution rate, polymorphic forms and stability are plays important role in preformulation study (Vilegave et al., 2013).

Melting point

Melting point of drug was determined by Open capillary

method.

Solubility Studies of drug (5-fluorouracil)

The solubility of a drug is the amount of the drug that dissolves in each solvent to produce a saturated solution at constant temperature and pressure. For making effective formulation drug molecule must have good aqueous solubility for better absorption. Solubility is not an independent parameter but it relies on several properties like crystal characteristics, temperature, pH, complexation, and molecular structure. Solubility of drug substance determines its systemic absorption and in turns its therapeutic efficacy. Solubility of drug was determined in different solvents (Coltescu et al., 2020).

Partition coefficient of 5-fluorouracil

Partition coefficient (Log P) value is defined as ratio of unionized drug distributed between aqueous and organic phase. Oil-water partition coefficient gives the idea about drug's ability to cross the lipidic membrane. Due to lipidic nature of biological membrane, the amount of drug absorbed depends heavily on its lipophilicity. It is the unionized form of molecule that has better lipophilicity and hence it has received so much importance (Schonsee and Bucheli, 2020).

50 mg of drug was taken in three separating funnels. The separating funnels were shaken for 2 hrs in a wrist action shaker for equilibration. Two phases were separated and the amount of the drug in aqueous phase was analysed spectrophotometrically. The partition coefficient of the drug in phase's was calculated by using formula:

$$Partition\ Coefficient = \frac{\text{Concentration of Drug in oil phase}}{\text{Concentration of drug in aueous phase}}$$

If the value of Log P is 0, it indicated that drug has equal distribution in water and partition solvent. Value of Log P less than 1 is indicative of higher water solubility and value greater than 1 is indicative of higher lipidic solubility. For optimum solubility and absorption, a proper hydrophilic lipophilic balance is necessary.

Determination of λmax

Take 5 mg of 5-fluorouracil and transferred into 5 ml volumetric flask. The volume was made up to 5 ml using respective solvent to obtain a solution that has a concentration 1000 µg/ml. 1 ml of this stock solution was taken and then diluted up to 10 ml to obtain a solution that has a concentration 100 µg/ml which is standard stock solution.

Standard calibration curve of 5-fluorouracil: Determination of absorption maximum (λ max)

From the above stock solution 0.3 ml sample was transferred into a 5 ml volumetric flask and the volume was make up to mark to prepare a concentration of 6 µg/ml. The sample was scanned by UV-VIS Spectrophotometer in the range of 200- 400 nm, using respective solvent as a blank. The wavelength corresponding to the maximum absorbance (max) was found (Jyothi and Padmaja, 2016).

Aliquots of 2, 4, 6, 8, 10,12 and 14 µg/ml prepared utilizing 100 µg/ml of 5-fluorouracil as standard solution. The absorbance of the resulting solution was measured 275nm against water blank. Calibration curve was prepared by plotting the absorbance vs concentration of drug.

FTIR study

Make KBr disc using 1 mg of drug and excipients in 100 mg of spectroscopic grade KBr which has been dried using IR lamp. Both KBr and 5-fluorouracil was mixed and subjected to hydraulic pressure to form disc. This disc was placed in FT-IR chamber. Infrared spectrum was recorded in the 4000 - 400 cm^{-1} region (Segall, 2019).

Preparation of Nano-sponges

5-fluoro uracil loaded nano-sponges were prepared by Emulsion Solvent Diffusion Method. For that we are using different proportions of ethyl cellulose (EC) and polyvinyl alcohol (PVA) in dichloromethane **(Table 1)**. The reaction mixture was stirred at 1000 rpm for 2 hr. filtered the reaction mixture and collected the nano-sponges and dried them in oven at 40°C for 24 hr. The dried Nano-sponges were stored in vacuum desiccators to ensure the removal of residual solvents (Srinivas and Sreeja, 2013).

Table 1. Composition of Nano-sponge

Ingredients (mg)	Formulation batches					
	F1	F2	F3	F4	F5	F6
5-fluorouracil (5-FU)	100	100	100	100	100	100
Ethyl cellulose	200	400	600	800	600	400
Polyvinyl alcohol (PVA)	200	400	600	800	1000	1200
Dichloromethane (DCM)	30	30	30	30	30	30
Distilled water	100	100	100	100	100	100

Characterization of Nano-sponges

Quantitative analysis: Entrapment Efficiency (EE)

UV spectrophotometric method was used to estimate entrapment efficiency of 5-fluorouracil nano-sponges. A calibration curve was plotted for 5-fluorouracil in methanolic HCl in the range of 3-18µg/mL (Beer's Lambert's range) at 275 nm. A good linear relationship was observed between the concentration of 5-fluorouracil and its absorbance. 100 mg of 5-fluorouracil nano-sponges of each batch were selected, powdered in a mortar and placed in 100 mL of methanolic HCl. 5-fluorouracil was extracted by centrifuging at 1000 rpm for 30 min, filtered and analyzed concentration from calibration curve data after necessary dilution (Jasim et al., 2020). Percentage entrapment was calculated as follows:

$$\%\ Entrapment\ efficiency = \frac{Actual\ drug\ conatin\ in\ nanosponges}{Theritical\ drug\ content} \times 100$$

Zeta Potential (ZP)

The surface charge of Nanosponge can be determined by using Zeta sizer. Zeta potential is a measurement of the overall charge of the particles in media and it indicates the stability of the particles in the sense that the higher the zeta potential the more stable the particles (Xu, 2008).

Scanning electron microscopy (SEM)

Surface morphology of nano-sponges was determined by using SEM technique, for which a drop of nano-sponges system was mounted on clear glass stub, air dried and coated with Polaron E 5100 Sputter coater (Polaron,) and visualized under Scanning Electron Microscope (SEM Leo 430,)(Patil and Mohite, 2016).

Formulation of 5-fluorouracil loaded Nano-sponges gel

Based on above characterization, formulation F4 was selected to incorporate into carbopol gel. The optimized F4 (1% w/w) was incorporated into carbopol as gelling agent (1%, w/v) in a 30:70 ratio of propylene glycol and deionized water. Further, methyl paraben (0.1%, w/w) was added as a preservative, transparency was achieved and pH was adjusted by adding triethanolamine **(Table 2)**. The developed gel was then continuously stirred on a shaft stirrer at 500 rpm for about 6 h and kept overnight to achieve complete hydration (Zhang et al., 2017).

Table 2. Composition of 5-fluorouracil loaded Nano-sponges gel

Ingredients	Formulation			
	G1	G2	G3	G4
Nanosponge (F4)	100	100	100	100
Carbopol (%)	0.15	0.25	0.55	0.75
Propylene glycol	1	1	1	1
Triethanolamine	Q.S.	Q.S.	Q.S.	Q.S.
Deionized water	10	10	10	10

Evaluation of Prepared Gel

Based on the physical and physicochemical characteristics formulation F4 was selected and incorporated into the polymeric gel. The developed gel was further evaluated.

Measurement of pH

The pH of 5-fluorouracil loaded nano-sponges based topical gel was checked by pH meter maintained at 25°C. The sample was tested in triplicate manner.

Determination of Viscosity

The viscosity of the developed NS based gel was measured using Brookfield viscometer. Viscosity was measured at 25°C at 100 rpm.

Spreadibility

The spreadibility test was performed by in-house fabricated apparatus. The apparatus consists of wooden block with a pulley at one end. The spread ability was measured by slip and drag of gel. A glass slide was fixed on wooden block and approximately one gram of gel was sandwiched between the two 5 × 20 cm glass plates. The top plate was laden with 100 g for 40 sec. The initial and final gel spreading diameters were noted and percentage spreadibility was calculated by following equation

$$Spreadability = \frac{D2 - D1}{D1} \times 100$$

Where; D1 was initial diameter of gel before weight load, and D2 was final diameter of gel after load.

Drug content analysis

Each nano-sponge loaded gel formulations were taken in 100 ml volumetric flask containing 20 ml of phosphate buffer pH 7.4 and stirred for 30 min. and allowed to stand for 24 hr. The volume was made up to 100 ml with phosphate buffer. Proper dilutions were made and the formulation was subjected to the spectrophotometric analysis. The content of drug was estimated spectrophotometrically by using standard curve plotted at λ_{max} at 275nm.

In vitro drug release of drug

The release of 5-FU from optimized nanosponge gel was determined by membrane diffusion technique using Franz diffusion cell. The nanosponge gel equivalent to (5% w/w of 5-FU) was taken in donor compartment. The donor and receptor compartment were separated by synthetic cellophane membrane. The synthetic cellophane membrane was mounted between donor and receptor compartment of

cell. The receptor medium was filled with phosphate buffer pH 7.4. The assembly was stirred at 200 rpm and receptor compartment was replenished with equal volume of phosphate buffer. Aliquots each of 1 ml was withdrawn periodically at an interval of 2, 4, 6, 8, 10, 12 and 24 hours and replaced by an equal volume of receptor medium. The aliquots were suitably diluted with receptor medium and analysed by UV visible spectrophotometer.

Kinetic studies

To analyze the in vitro release data various kinetic models were use to describe the release kinetics. The zero-order rate Eq. (1) describes the systems where the drug release rate is independent of its concentration. The first order Eq. (2) describes the release from system where release rate is concentration dependent. Higuchi (1963) described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion (Eq. 3) (Higuchi, 1963). The results of in vitro release profile obtained for all the formulations were plotted in modes of data treatment as follows:

$$Zero\ order\ kinetic\ model = \frac{Cumulative\ perecent\ of\ drug\ released}{Time} \quad Eq.1$$

$$A_t = A_0 - K_0 t$$

A_t = Drug release at time't'

A_0 = Initial drug concentration.

K_0 = Zero- order rate constant (hr-1)

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys Zero – order kinetics and its slope is equal to Zero order release

constant K_0.

$$First\ order\ kinetic\ model = \frac{Log\ cumulative\ percent\ drug\ remaining}{Time} \quad Eq.2$$

$\text{Log } C = \log C_0 - K_t / 2.303$

C = Amount of drug remained at time 't'; C_0 = Initial amount of drug; K = First - order rate constant (hr-1).

$$Higuchi's\ model = \frac{Cumulative\ percent\ drug\ released}{Square\ root\ of\ time} \quad Eq.1$$

$Q = [D\epsilon / \tau (2A - \epsilon Cs) Cst]^{1/2}$

Q = Amount of drug release at time 't'; D = Diffusion coefficient ofthe drug in the matrix.

A = Total amount of drug in unit volume of matrix; Cs = Solubility of drug in matrix

ϵ = Porosity of matrix; τ = Tortuosity; t = Time (hrs.) at which q amount of drug is released.

Above equation can be simplified as if we assume, that 'D', 'Cs' and 'A' are constant. Then

equation: becomes

$Q = Kt^{1/2}$

When the data plotted as log cumulative percent drug remaining versus time, yields a straight

line, indicating that the release follows first order kinetics. The constant 'K1' can be obtained When the data plotted as log cumulative percent drug remaining versus time, yields a straight line, indicating that the release follow first order kinetics (Higuchi, 1963). The constant 'K1' can be obtained by multiplying 2.303 with the slope value.

Stability studies

The optimized formulation of 5-FU loaded nanosponge gel was packed in aluminium collapsible tubes and subjected to stability studies at 25°C± 5°C and 40% RH and 40°C± 5°C and 70% RH for a period of 3 months. Formulations were evaluated at periodic intervals for pH, viscosity, spreadibility and drug release profiles (Huynh-Ba and Dong, 2020).

Results and Discussion

Preformulation studies

Melting Point of 5-FU was found to be 280±3°C. Solubility of 5-FU shown in **Table 3**. Partition coefficient of 5-FU was found to be 1.2.

Characterization of Nano-sponges

Quantitative analysis (Entrapment Efficiency)

Entrapment efficiency of all the batches of 5-fluorouracil nano-sponges was evaluated and the best formulation was selected for further formulation of nano-sponges gel based on entrapment efficiency of the nano-sponges **(Table 4 and Figure 1)**. From the entrapment efficiency studies of 5-FU nano-sponges, it was observed that formulation F4 showed better entrapment of drug into the nano-sponges. So, it was selected for further preparation of nano-sponges gel.

Zeta Potential

Zeta potential of formulation was shown in **Figure 2.**

Scanning Electron Microscopy

Scanning Electron Microscope (SEM) is also used to

Table 3. Solubility of 5-Fluorouracil

S. No.	Solvents	Solubility status
1.	Methanol	Freely soluble
2.	Ethanol	Soluble
3.	Chloroform	Sparingly soluble
4.	Water	Soluble

of 5-fluorouracil

Table 4. Entrapment efficiency of 5fluorouracil nano-sponges

S. No.	Formulation batch	Entrapment Efficiency (%)
1.	F1	50.23
2.	F2	64.85
3.	F3	72.65
4.	F4	78.67
5.	F5	88.46
6.	F6	79.28

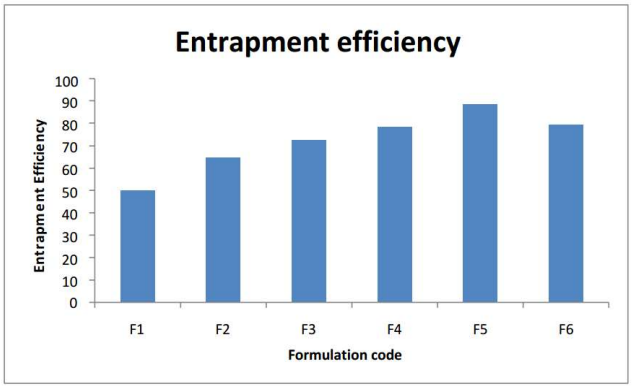

Figure 1: Entrapment efficiency of different formulations of 5-FU

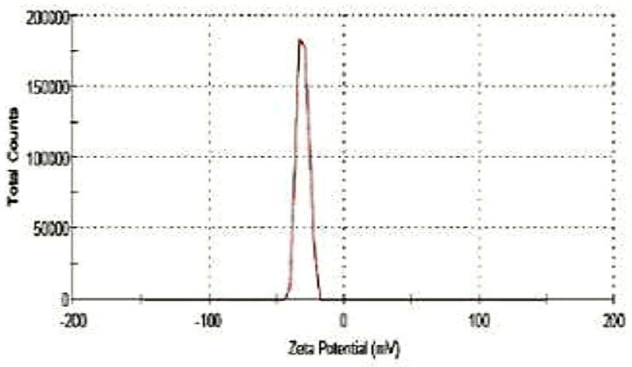

Figure 2. Zeta Potential of formulations

characterize the surface morphology of the nanosponges **(Figure 3)**. One drop of nanosponges is mounted on a clear glass stub, it is air dried and visualized under Scanning electron microscope.

Evaluation of Prepared Gel

Based on the physical and physicochemical characteristics, F4 was selected and incorporated into the polymeric gel. The developed gel was further evaluated and shown in **Table 5**. pH of the formulation G3 was found to be 7.36±0.25-7.94±0.20, That suits the skin pH indicating skin compatibility. Viscosity was found in range of 7257±1.57 to 8438±2.87 cp. Also the viscosity increases with increase in pH. And spreadibility was found to be 11.54±0.06 to 11.94±0.08 g.cm/sec.

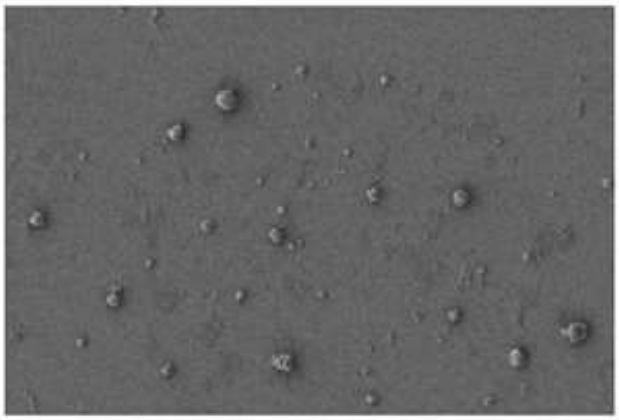

Figure 3. SEM images of 5-Fluorouracil nanosponges

Table 5. Evaluation of 5-fluorouracil nanosponges gel

Parameters	Formulations			
	G1	G2	G3	G4
pH	7.45±0.15	7.36±0.25	7.94±0.20	7.64±0.18
Viscosity (cp)	7459±1.67	8367±2.67	8438±2.87	7257±1.57
Spreadibility (g.cm/sec)	11.65±0.04	11.54±0.06	11.85±0.05	11.94±0.08

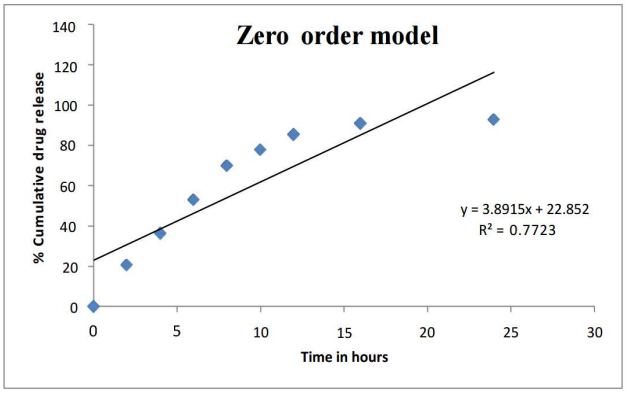

Figure 4. Zero order model of G3 formulation

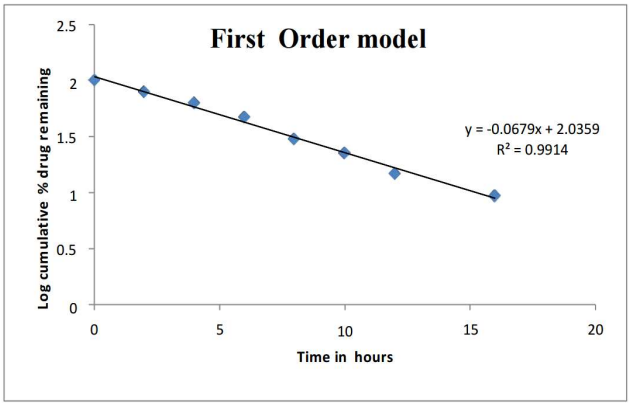

Figure 5. First order model of G3 formulation

In vitro drug release of 5-fluorouracil nanosponges gel

The In-vitro diffusion study was taken by using franz diffusion cell which shows cumulative % drug release of 5-fluorouracil gel formulation. Among all the formulations,

G3 was selected for in-vitro drug release study because it showed highest drug content **(Figure 6)**.

Release kinetic studies

Kinetics studies of the G3 formulation shown in table 7. Zero order kinetic model refers to the process of constant drug release from a drug delivery device independent of the concentration. The zero-order graph of G3 formulation showed the constant drug release from the nanosponges gel, the results of the zero-order model was found to be y =3.891x + 22.85, R2 = 0.772 (Figure 4). The first order kinetic model describes the release from system where release rate is concentration dependent (Figure 5). The results of first order kinetic model were found to be y = -0.067x + 2.035, R^2 = 0.991 that showed the release of drug which is concentration dependent. The Higuchi model is used to describe the limits for transport and drug release. The Higuchi model of patches was found to be 22.06x - 1.052, R^2 =0.930 (Figure 6).

Stability studies

Stability studies were performed for the best formulation of nanosponges gel (G3) at two different conditions. pH for G3 formulation was found to be 7.56 and 7.54 for 90 days at 25°C and 40% RH and 40°C and 70% RH, respectively. The variation could be due to storage and imbibing of nanosponges with gel. % drug release of G3 formulation for 90 days was found to be 89.4 and 89.8% at 25°C and 40% RH and 40°C and 70% RH **(Table 8)**.

Table 6. *In vitro* drug release of G3 formulation of 5-fluorouracil nanosponges gel

S. No.	Time in hours	% Cumulative drug release
1.	2	20.46
2.	4	36.03
3.	6	52.67
4.	8	69.70
5.	10	77.45
6.	12	85.23
7.	16	90.67
8.	24	92.56

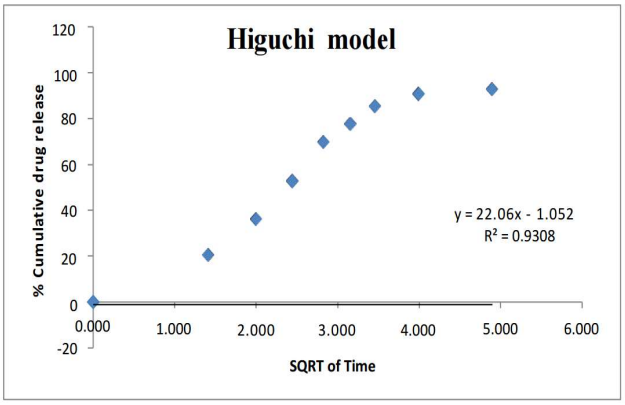

Figure 6. Higuchi model of G3 formulation

Table 7. Release kinetics study of G3 formulation

Formulation	Model	Kinetic parameter values
G3	Zero order	y = 3.891x + 22.85 R2 = 0.772
	First order	y = -0.067x + 2.035 R^2 = 0.991
	Higuchi	y = 22.06x - 1.052 R^2 = 0.930

Table 8. Evaluation of optimized batch G3 at different time intervals after storage under 40 ± 20C/ 75 ± 5% RH

Time	Stability condition / parameter					
	25°C± 5°Cand 40% RH			40°C± 5°C and 70% RH		
	pH	Viscosity	% Drug release	pH	Viscosity	% Drug release
30 days	7.23±0.23	7423±1.54	90.7	7.35±0.20	7548±1.58	88.4
60 days	7.37±0.24	7535±1.54	89.3	7.45±0.22	7646±1.54	87.5
90 days	7.56±0.26	7635±1.57	89.4	7.54±0.23	7794±1.56	89.8

Conclusion

In this work we prepare and evaluate 5-fluoro uracil loaded nanosponges gel. This formulation will deliver therapeutically effective amount of drug across the skin when it placed on skin. Nanosponges was prepared and evaluated for entrapment efficiency, Zeta potential and SEM. From evaluation results, it was observed that among six formulations, F4 formulation showed better entrapment of drug, so it was further used for gel formulation. Incorporation of carbapol was used for the nanosponges gel formulation. Total 4 formulations were prepared and evaluated against different parameters like pH determination, viscosity, spreadibility, drug content and in vitro drug release. From all the results of the evaluation parameters G3 was found to contain 94% drug content and drug release was found to be 92%.

Acknowledgment

The authors gratefully acknowledge to Truba Institute of Pharmacy Bhopal, India and PBRI research lab Bhopal, India for providing facilities and platform for the research work.

References

Alongi J, Poskovic M, Frache A, Trotta F. 2011. Role of β-cyclodextrinnanosponges in polypropylene photooxidation. Carbohydrate Polymers, 86(1): 127-135.

Coltescu AR, Butnariu M, Sarac I. 2020. The importance of solubility for new drug molecules. Biomedical and Pharmacology Journal, 13(2).

Higuchi T. 1963. Mechanism of Sustained-Action Medication. Theoretical Analysis of Rate of Release of Solid Drugs Dispersed In Solid Matrices. Journal of Pharmaceutical Sciences 52:1145-9.

Huynh-Ba K, Dong MW. 2020. Stability studies and testing of pharmaceuticals: An overview. LCGC North America, 38(6), 325-336.

Jasim IK, Abd Alhammid SN, Abdulrasool AA. 2020. Synthesis and Evaluation of β-cyclodextrin Based Nanosponges of 5-Fluorouracil Using Ultrasound Assisted Method. Iraqi Journal of Pharmaceutical Sciences, 29(2), 88-98.

Jyothi BJ, Padmaja G. 2016. Uv spectrophotometric method for estimation of new drug, daclatasvir dihydrochloride. International Research Journal of Pharmacy, 7(9):1-3.

Nichols JW, Bae UH. 2012. Odyssey of a cancer nanoparticle: from injection site to site of action. Nano Today, 7(6): 606-618.

Patil BS, Mohite SK. 2016. Formulation Design & Development of Artesunate Nanosponge. European Journal of Pharmaceutical and Medical Research, 3(5): 206-211.

Prabhakar D, Sreekanth J, Jayaveera KN. 2013. Transdermal drug delivery patches: A review. Journal of Drug Delivery and Therapeutics, 3(4), 231-221.

Sanvicens N, Marco MP. 2008. Multifunctional nanoparticles–properties and prospects for their use in human medicine. Trends in Biotechnology, 26(8): 425-433.

Schonsee CD, Bucheli TD. 2020. Experimental determination of octanol–water partition coefficients of selected natural toxins. Journal of Chemical & Engineering Data, 65(4): 1946-1953.

Segall, Ines A. 2019. Preformulation: The Use of FTIR in Compatibility Studies. Journal of Innovations in Applied Pharmaceutical Science, 4: 1-6.

Selvamuthukumar S, Anandam S, Krishnamoorthy K, Rajappan M. 2012. Nanosponges: A novel class of drug delivery system-review. Journal of Pharmacy & Pharmaceutical Sciences, 15(1): 103-111.

Srinivas P, Sreeja K. 2013. Formulation and evaluation of voriconazole loaded nanosponges for oral and topical delivery. International Journal of Drug Development and Research, 5(1):55-69.

Trotta F, Mele A (Eds.). Nanosponges: Synthesis and Applications. John Wiley Sons. 2019.

Vilegave K, Vidyasagar G, Chandankar P. 2013. Preformulation studies of pharmaceutical new drug molecule and products: An Overview. The American Journal of Pharmacy. 1(3): 1-20.

Vyas A, Saraf S, Saraf S. 2008. Cyclodextrin based novel drug delivery systems. Journal of Inclusion Phenomena and Macrocyclic Chemistry, 62(1): 23-42.

Xu R. 2008. Progress in nanoparticles characterization: Sizing and zeta potential measurement. Particuology, 6(2):112-115

Zhang Y, Gao W, Chen Y, Escajadillo T, Ungerleider J, Fang RH, Zhang L. 2017. Self-assembled colloidal gel using cell membrane-coated nanosponges as building blocks. ACS Nano, 11(12):11923-11930.