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Formulation and Evaluation of Dapsone Nanosponge Topical Gel

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Abstract
Recent advances in nanotechnology paved path for design of nanogels with many potential applications in the field of nanomedicine. Nanogels being dispersions of hydrogel nanoparticles or nano sponges offer high drug loading compared to other nanocarriers and are thus suitable for solving issues related to stability, solubility and delayed release of actives and to formulate drug delivery systems for various administration routes besides the oral one. Development of Nano sponges as topical drug delivery systems is presented in this dissertation. where we formulated Dapsone nano sponge based topical gel using ethyl cellulose as polymer and polyvinyl alcohol as surfactant with different concentration. Which were evaluated for percentage yield, drug entrapment efficiency, surface morphology, particle size analysis and *in-vitro* drug release among all 6 different formulations F5 batch considered as the best with 76% of drug entrapment efficiency and with greater percentage drug release of 96.80% at the end of 12hrs. From the SEM analysis its concluded that nano sponges are spherical, discreet with smooth surface, and particle size was found to be 91.22 (d.nm) by zeta sizer. The nano sponges of the best formulation F5 was loaded into the Carbopol 394P gel which were evaluated for viscosity, spreadability, pH, extrudability, drug content, *in-vitro* drug diffusion study, release kinetics and stability studies. Finally, we concluded that prepared dapsone nano sponge topical gel shows promised drug release and good stability.

Keywords
Dapsone nano sponge, Topical gel, Ethyl cellulose.

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INTRODUCTION:
An ideal drug therapy achieves effective concentration of drug at the target site for a specified period of time in order to minimize general and local side effects. Nanotechnology resulted in multifarious formulations like nanoparticles, Nano capsules, nanospheres, nanosuspensions, nanocrystals, nano-erythosomes etc. Nanotechnology is a technology relates to creation and manipulation. Nanoparticles are a newer development which is accessible in several forms like polymeric nanoparticles, solid-lipid nanoparticles, nano emulsions, nano sponges, carbon nanotubes, micellar systems, dendrimers etc.[2] Nano sponges are porous polymeric delivery systems that are small spherical particles with large porous surface. These are used for the passive targeting of cosmetic agents to skin, there by achieving major benefits such as reduction of total dose, retention of dosage form on the skin and avoidance of systemic absorption.[3]

NANOSPONGES:

Nano sponges are nano sized particles designed to look like red blood cells and protect the body. Nano sponges are tiny sponges with a size of about a virus (250nm – 1mm), Which consists of cavities that can be filled with a wide variety of drugs. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface to release the drug in a controlled and predictable manner. The sponge acts as a dimensional network or scaffold, which consist of the backbone known as long-length polyester.

Advantages of Nanosponges[7]

- Targeted site-specific drug delivery.
- Can be used to mask unpleasant flavours and to convert liquid substances to solids.
- Less harmful side effects (since smaller quantities of the drug have contact with healthy tissue).
- Nano sponge particles are soluble in water, so the hydrophobic drugs can be encapsulated within the nano sponge, after mixing with a chemical called an adjuvant reagent.
- Particles can be made smaller or larger by varying the proportion of cross-linker to the polymer.
- Easy scale-up for commercial production.
- The drug profiles can be tailored from fast, medium to slow release, preventing over or under-dosing of the therapy.
- Improved stability, increased elegance and enhanced formulation flexibility.

Disadvantages:

1. Nanosponges include only small molecules.
2. Nanosponges could be either para-crystalline or crystalline form.
3. Depend only upon loading capacities of drug molecules.

FACTORS AFFECTING NANOSPONGE FORMULATION

1. Type of Drug
2. Type of Polymer used
3. Temperature
4. Method of preparation nanosponge
5. Degree of substitution

METHODS OF PREPARATION OF NANOSPONGES[8]

Emulsion solvent diffusion method:

In this method the two phases used are organic and aqueous. Aqueous phase consists of polyvinyl alcohol and organic phase include drug and polymer. After dissolving drug and polymer to suitable organic solvent, this phase is added slowly to the aqueous phase and stirred for two or more hours and then nanosponges are collected by filtration washed and then dried in air at room temp or in vacuum oven 40^{o}c for 24 hrs.

Quasi-emulsion solvent diffusion:

The nano sponges can also be prepared by quasi-emulsion solvent diffusion method using the different polymer amounts. To prepare the inner phase, Eudragit RS100 was dissolved into a suitable solvent. Then, the drug can be added to the solution and dissolved under ultrasonication at 35^{o}c. The inner phase was poured into the PVA solution in water (outer phase). Following 60min of stirring, the mixture is filtered to separate the nano sponges. The nano sponges are dried in an air-heated oven at 40^{o}c for 12 hrs.

Solvent method:

Mix the polymer with a suitable solvent, in particular in a polar aprotic solvent such as di methyl formamide, di methyl sulfoxide. Then add this mixture to excess quantity of the crosslinker, preferably in crosslinker/polymer molar ratio of 4 to 16. Carry out the reaction at temperature ranging from 10°C to the reflux temperature of the solvent, for time ranging from 1 to 48h. Preferred crosslinkers are carbonyl compounds (Di methyl carbonate & Carbonyl di imidazole). After completion of the reaction, allow the solution to cool at room temperature, then add the product to large excess of bi distilled water and recover the product by filtration under vacuum and subsequently purify by prolonged Soxhlet extraction with ethanol. Dry the product under vacuum and grind in a mechanical mill to obtain homogeneous powder.

Ultra sound-Assisted synthesis[9]:

In this method nanosponges can be obtained by reacting polymers with cross-linkers in the absence of solvent and under sonication. The nanosponges obtained by this method will be spherical and uniform in size. Mix the polymer and the cross-linker in a particular molar ratio in a flask. Place the flask in an ultrasound bath filled with water and heated to 90°C. Sonicate the mixture for 5hours. Then allow the mixture to cool and break the product roughly. Wash the product with water to remove the non-reacted polymer and subsequently purify by prolonged Soxhlet extraction with ethanol. Dry the obtained product under vacuum and store at 25°C until further use.

TOPICAL DRUG DELIVERY SYSTEMS

Topical delivery is an attractive route for local and systemic treatment. The delivery of drugs onto the skin is recognized as an effective means of therapy for local dermatologic diseases. It can penetrate deeper into skin and hence give better absorption. Topical application has many advantages over the conventional dosage forms. In general, they are deemed more effective less toxic than conventional formulations due to the bilayer composition and structure.

Topical formulations have three main functions:

- To help hydrate skin because of their emollient properties.
- To protect from external environment or heal an intact or injured area of the skin.
- To deliver medication to the skin.

GEL[13]

The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. Gels consist of two-phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains.

CHARACTERISTICS OF GELS

Swelling: - When a gelling agent is kept in contact with liquid that solvates it, then an appreciable amount of liquid is taken up by the agent and the volume increases. This process is referred to as swelling.

Syneresis: Many gels often contract spontaneously on standing and exude some fluid medium. This effect is known as syneresis.

Ageing:

Colloidal systems usually exhibit slow spontaneous aggregation. This process is referred to as ageing. In gels, ageing results in gradual formation of a denser network of the gelling agent.

Structure

The rigidity of a gel arises from the presence of a network formed by the interlinking of particles of the gelling agents. The nature of the particle and the stress, straightening them out and lessening the resistance to flow.

APPLICATIONS OF GEL

- As delivery systems for orally administered drugs.
- To deliver topical drug applied directly to the skin, mucous membrane or the eye.
- As long-acting forms of drug injected intramuscularly.
- As binders in tablet granulation, protective colloids in suspensions, thickeners in oral liquid and suppository bases.
- In cosmetics like shampoos, fragrance products, dentifrices, skin and hair care preparations.

Dapsone[09,10]

Dapsone is an antibacterial and used from 1940s for the betterment of leprosy and skin disorders such as dermatitis herpetiformis and nodulocystic acne.

Pharmacology of dapsone

Chemically, dapsone is an aniline derivative. As a sulfone, it shows the structure of a sulphur atom linking to two carbon atoms (Fig. 1). Solubility of dapsone varies over a wide range depending on the solvent used (e.g., water, 0.2 mg/mL vs. methanol, 52 mg/mL). Following oral administration, dapsone is almost completely absorbed from the gut with bioavailability exceeding 86 %. Peak serum concentrations are attained within 2–8 h. After ingestion of a single 50–300 mg dose of dapsone, maxi- mum serum concentrations range from 0.63 to 4.82 mg/L [2, 165, 181]. Under steady-state conditions,100 mg/day (the dose most frequently used) results in serum concentrations of 3.26 mg/L (maximum) and 1.95 mg/L (after 24 h).

Antimicrobial activity:

As an antimicrobial agent, dapsone is bacteriostatic in action. It inhibits the synthesis of dihydrofolic acid through by competing with para-aminobenzoic acid for the active site of dihydropteroate synthetase, thus resembling the action of sulphonamides. Sulfones were found to sup- press the growth of various pathogenic bacteria such as streptococci, staphylococci, pneumococci, mycobacteria, and other strains. The mechanism of action of topical dapsone in the treatment of acne vulgaris may result from a combination of both antiinflammatory and antimicrobial effects. In vitro, dapsone has some antibacterial activity against Propionibacterium acnes. Owing to its antimicro- bial activities, dapsone is clearly playing a role in the treatment of certain infectious diseases.

The aim of this study is to prepare and evaluate the gel containing nanosponges of dapsone.

DRUG PROFILE

Dapsone[09]

Dapsone is an aniline derivative belonging to the group of synthetic sulfones, Dapsone is an antibacteial and used for the betterment of leprosy and skin disorders such as dermatitis herpetiformis and nodulocystic acne.

Structural formula:

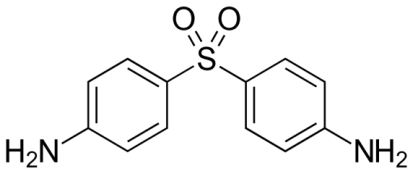

Fig. No.1 Structural formula of dapsone

IUPAC Name :4-(4-aminophenyl)sulfonylaniline.
Molecular Formula : $C_{12}H_{12}N_2O_2S$
Molecular mass : 248.3 g/mol
Description : A white crystalline powder , odorless.
BSC class : class II drug
Solubility : Freely soluble in ethanol and methanol, and slightly soluble in acetone and very slightly soluble in water.
Melting point : 175.5°C
Half-life : 30hrs
Dose : leprosy- 50 to 100mg per Day (6 to 10mg/kg per week) & Topical dose-5-7.5%.

METHODOLOGY

PREFORMULATION STUDIES[10]

Preformulation study is the first step in the rationale development of dosage form of a drug substance. The overall objective of preformulation studies is to generate information useful to the formulator in developing a stable and bioavailable dossage form which can be mass produce.

- **Organoleptic charecterstics:**
  The colour, odour, of Dapsone will be charectrized by descriptive technology.
- **Solubility:**
  The solubility study was conducted by taking excess amount of drug in 10ml of solvent (water & 7.2 phosphate buffer) Then the sample were kept in the water bath shaker and agitated for 24hrs at 37±5°C, the samples were analyzed spectrophotometrically at λmax 293nm.
- **Melting point**
  Melting point of Dapsone was determined by open capillary method fine powder of Dapsone was filled in a glass capillary tube (sealed at one end). The capillary tube was tied to a thermometer and a was placed in Thiel's tube containing liquid paraffin which was further placed on flame the temperature at which the powder starts melting was noted.

SPECTROSCOPIC STUDIES

- **Construction Of Standard Calibration Curve of Dapsone[11]:**
  Preparation of 7.2 pH phosphate buffer: Dissolve 34.7ml of 0.2N sodium hydroxide and 50ml of 0.2ml potassium dihydrogen phosphate in distilled water and make volume upto 200ml with distilled water.
- **Determination of λ max:**
  Most of the drugs absorb light in UV wavelength region (200-400nm) hence λmax was determined by using UV spectrophotometer. The solution containing 10µg/ml concentration of Dapsone was prepared and scanned over range of 200-400nm against 7.2 pH phosphate buffer as blank using double beam UV spectrometer. The maximum absorbance of wavelength in the graph was considered as λmax of the pure drug.
- **Preparation of standard stock solution and standard calibration curve of Dapsone:**

100mg of dapsone was accurately weighed and transferred into a 100ml volumetric flask. It is then dissolved in small quantity of 7.2pH phosphate buffer and the volume is made upto 100ml using same buffer to get a solution concentration of 1000µg/ml as stock solution A. 10ml of stock solution A was again diluted with 100ml 7.2 pH phosphate buffer to get a stock solution B of 100µg/ml. Then buffer dilutions were made with same medium by pipetting out 2ml, 4ml, 6ml, 8ml and 10ml to get the solution concentration ranging from 2µg/ml to 10µg/ml.

DRUD-EXCIPEINT COMPATIBILITY STUDY[12]

In the preparation of topical gel containing nanosponges, drug and polymer may interact as they in close contact with each other, which could lead to the instability of drug. Preformulation studies regarding the drug-polymer interaction are therefore very critical in selecting appropriate polymers. FTIR spectroscopy helps to confirm the identification of drug and detects the interaction of the drug with the carriers. FTIR spectroscopy of pure drug (Dapsone). Physical mixture of drug and polymers and Dapsone nanosponge topical gel was carried out using FTIR to check the compatibility between drug and polymer.

The FTIR spectra of the drug with polymers were compared with the standard FTIR spectrum of the pure drug.

Procedure: The pure drug, pure polymer, dug and polymer and physical mixture of drug, polymer and other excipients were prepared and scanned from 4000-400 cm^{-1} in FTIR spectrometer. The IR spectrum of pure Dapsone and formulated nanosponges topical gel were recorded by FTIR spectrometer.

Formulation of Dapsone nanosponges

• **Emulsion Solvent Diffusion Method:**

Nanosponges can be prepared by using different proportions of ethyl cellulose (EC) and polyvinyl alcohol (PVA). The dispersed phase containing Ethyl cellulose and drug was dissolved in 20ml dichloromethane and slowly added to a definite amount of polyvinyl alcohol in 100ml of aqueous continuous phase. The reaction mixture was stirred at 2000 rpm for 2hrs. The Nanosponges formed were collected by filtration and dried in oven at 40^0c for 24hrs.

Ingredients	F1	F2	F3	F4	F5	F6
DAPSONE: EC (mg)	100:100	100:100	100:150	100:150	100:200	100:200
PVA (%W/V)	0.2	0.3	0.2	0.3	0.2	0.3
Dichloromethane (ml)	20	20	20	20	20	20
Distilled water up to	100	100	100	100	100	100

Formula for preparation of Nanosponge

Development of Dapsone Nanosponge loaded gel:[13]

Initially, the polymer Carbopol 934P (100 mg) was moistened insolvent i.e., water (5 ml) for the gel for 2-3 hrs and dispersed by constant stirring at 600 rpm with aid of magnetic stirrer to get smooth dispersion. Then to the above dispersion added Triethanolamine (2%v/v) to neutralize the pH. The previously prepared Dapsone nanosponge (amount equivalent to 10% of drug) and Propylene glycol as permeability enhancers were added to the above aqueous dispersion and make up the volume to 100 ml with distilled water.

Characterization of nanosponges.

1.Percentage yield:

The Dapsone nanosponges obtained after drying was weighed. Percentage yield value was calculated using the equation below,

$$\text{Percentage yield} = \frac{\text{Weight of nanosponges obtained}}{\text{Total weight of drug and polymer}} \times 100$$

2.Determination of drug entrapment efficiency[14]**:**

The entrapment efficiency was determined by measuring the concentration of the drug in the supernatant after centrifugation. The unentrapped Dapsone was determined by adding 10 mg Dapsone loaded Nanosponge in 10 ml of 7.2 pH phosphate buffer and then the dispersion were centrifuged at 9,000rpm for 30minutes in order to separate entrapped from the unentrapped drug. The free drug concentration in supernatant layer after centrifugation is determined at λmax (293nm) using UV Spectrophotometer The percentage entrapment efficiency (%EE) is calculated by following formula:

$$\%\text{EE} = \frac{\text{Weight of Initial drug} - \text{Weight of free drug}}{\text{Weight of Initial drug}} \times 100$$

SEM analysis.:

The samples for the scanning electron microscope (SEM) analysis were prepared by placing the nanosponges on one side of an adhesive stab. Then the nanosponges were coated with gold/palladium before microscopy, Finally the morphology size of the nanosponges measured under the SEM.

4.Determination of zeta potential[:]

Zeta potential can be defined as the difference of potential between two layers (dispersion medium and immobile layer) of fluid locked up with dispersed particles. Zeta potential can be measured by using instrument zeta sizer, which is the measure the surface charge of Nan sponges. Zeta potential is widely used for quantification of the magnitude of the electrical surface charge at the double layer.

5.*In-vitro* drug release study of formulated nanosponges[15]**:**

The *in-vitro* release of Dapsone Nanosponge was evaluated for all the batches by Dialysis Bag diffusion

technique. The release studies of Dapsone Nanosponge were performed in Phosphate buffer of pH 7.2, 10mg equivalent Dapsone Nanosponge were suspended in 10ml of phosphate buffer pH 7.2 mixture and placed in the dialysis bag (donor compartment) and sealed at both ends. The dialysis bag were immersed in receptor compartment containing 100ml of buffer, which was stirred at 100rpm and maintain 37°C.The Samples were taken from the receptor compartment and the same amount was replaced with the diffusion medium. Samples are taken upto12hrs. Dapsone in the samples were measured spectrophotometrically at λ 293nm.

Evaluation of Dapsone nanosponeged gel.

1. Determination of Viscosity.[16]

The measurement of viscosity of the prepared gel was done with Brookfield viscometer. The reading was taken at 100 rpm using spindle no. 6

2. Determination of spreadability.[17]

The spreadability of the gel formulation was determined, by measuring diameter of lg gel between horizontal plates (20 x20cm) after 1 min. The standardized weight tied on the upper plate was 125 g. The spreadability was calculated by using the following formula.

$$S = \frac{m.l}{t}$$

Value "S" is spredability, m is the weight tied to the upper slides, "l" is the length of glass slide, and "t" is the time taken.

3. Determination of pH.[18]

The pH of the gels was determined using digital pH meter. The readings were taken for average of 3 times.

4. Extrudability.[19]

In this method, the formulated gel were filled in standard capped collapsible aluminum tube and sealed by crimping to the end. The weights of the tubes were recorded. The tubes were placed between two glass slides and were clamped. 500g of weight was placed over the slides and then cap was removed. The amount of the extruded gel was collected and weighed. The percent of the extruded gel was calculated.

5. Determination of drug content of gel.[20]

A quantity (100 mg) of the gel was dissolved in 100 ml of phosphate buffer of pH 7.2. The volumetric flask containing gel solution was shaken for 2 h on a mechanical shaker to allow the drug to dissolve completely. The solution was filtered and drug content determined spectrophotometrically at 293nm using phosphate buffer (pH 7.2) as blank.

6. *In-vitro* drug diffusion study.[21]

The apparatus consists of a glass cylinder open at both ends. A dialysis membrane soaked in distilled water (24 h before use) is fixed to the one end of the cylinder with the aid of an adhesive. Gels equivalent to 10mg of Dapsone is taken inside the cell (donor compartment) and the cell is immersed in a beaker containing 100ml of 7.2 pH phosphate buffer, act as receptor compartment. The whole assembly is fixed in such a way that the lower end of the cell containing gel is just above the surface of the diffusion medium (1-2 mm deep) and the medium was agitated using a magnetic stirrer at the temperature 37 ± 0.5°C. Aliquots (5 ml) are withdrawn from the receptor compartment periodically and replaced with same volume with fresh buffer. The samples were analyzed by using UV-visible spectrophotometer at 293 nm.

7 *In-vitro* drug release kinetics.[22]

The data obtained from *in-vitro* dissolution were applied to various kinetic models such as zero order kinetics, first order kinetics, Higuchi and peppa's equations to understand the mechanism of release of drug from nanosponges.

stability studies. [23]

Dapsone nanosponge gel were subjected to stability studies for 60 days at an accelerated condition at 40±2˚C / 75±5% RH due to lack of time to carry out for 6 months as per new ICH guidelines. gel were evaluated for drug content and in-vitro drug dissolution studies.

RESULT:

Preformulation studies of Dapsone

Properties	Reported		Observed	
Appearance	White or creamy white		Creamy white	
Crystallinity	Crystalline powder		Crystalline powder	
Taste	Slightly bitter taste		Slightly bitter taste	
Odour	Odorless		Odorless	
Solubility	Water 7.2pH PBS	0.38mg/1ml 0.5mg/1ml	Water 7.2pH PBS	0.35mg/1ml 0.5mg/ml
Melting range	175-176°C		175°C	
Identification (UV)	293nm		293nm	

Table no: - 01

Determination of λ max

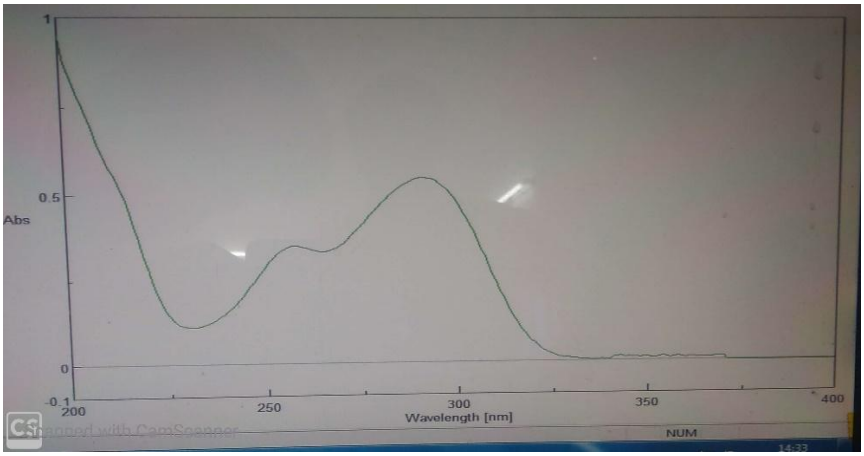

Figure No. 2

This was performed by using UV spectrophotometer by using PBS (pH 7.2) as medium. The spectrum of dapsone (10µg/ml) in PBS (pH 7.2) showed the peak at 293nm. The absorption maximum (λmax) of 293nm was selected for the present study.

Standard calibration curve for Dapsone

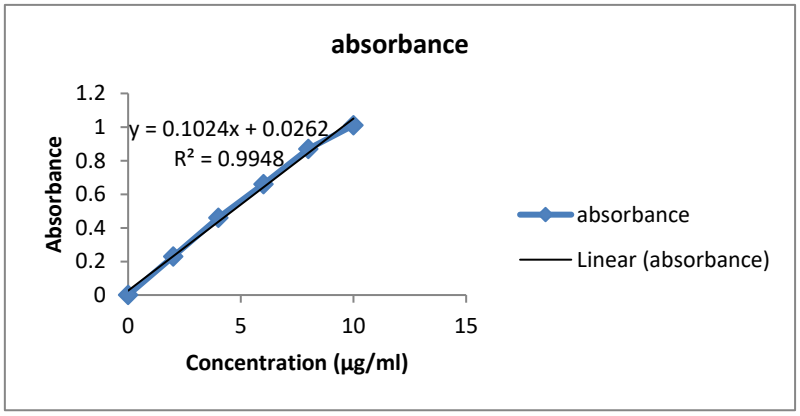

Figure No. 3 The standard calibration curve of Dapsone was obtained in the range of 2-10µg/ml measured at the wavelength of 293nm.

DRUD-EXCIPEINT COMPATIBILITY STUDY

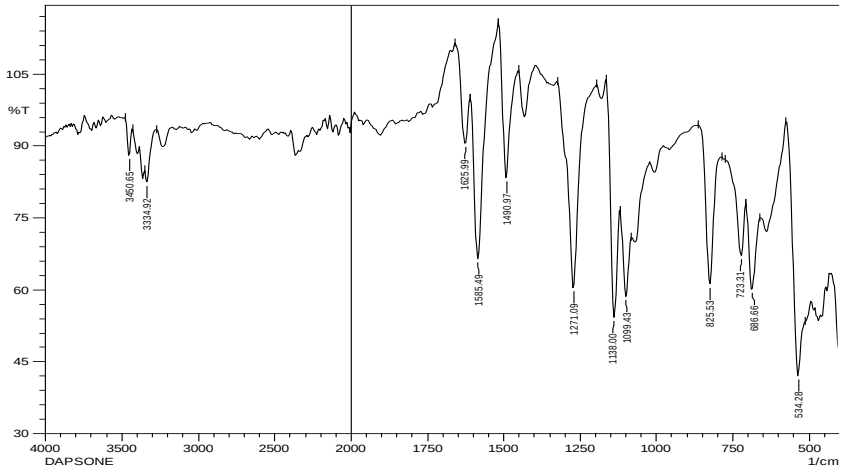

Figure No. 4

FTIR spectra of Dapsone

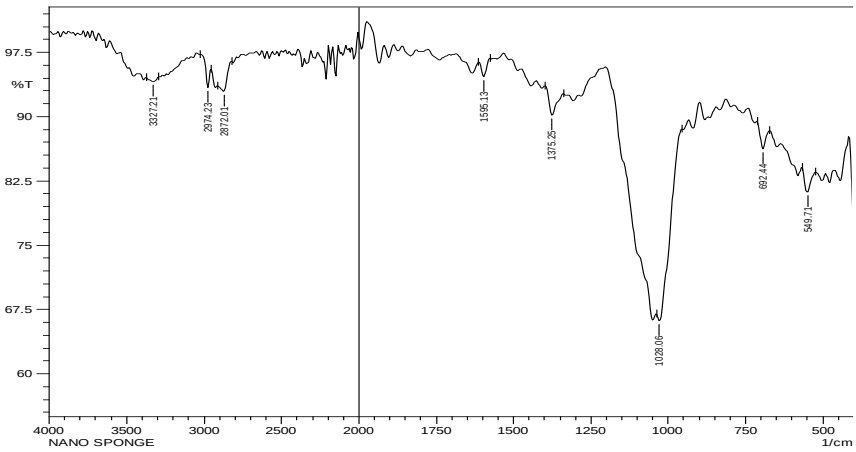

Figure No. 5

***In-vitro* drug release study**

Time (hrs)	% Cumulative Drug Release					
	F1	F2	F3	F4	F5	F6
0	-	-	-	-	-	-
1	11.80	12.28	13.18	12.40	12.84	13.28
2	20.64	20.86	21.46	21.10	21.90	21.78
3	31.20	31.80	32.18	32.10	32.66	32.28
4	42.92	43.10	43.24	43.30	43.80	43.40
5	53.62	53.80	54.12	54.80	55.96	55.20
6	62.84	65.20	61.46	63.48	66.40	62.58
7	71.60	72.20	73.28	71.56	78.90	71.64
8	82.64	81.88	84.26	82.36	89.50	84.64
12	95.46	94.40	95.28	94.88	96.80	94.20

In-vitro drug release study of formulated nanosponges

Table no: - 02

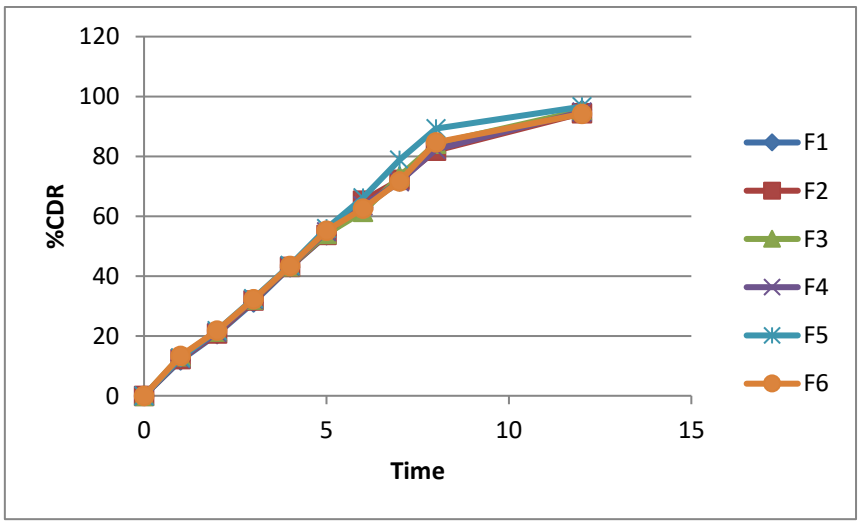

Figure No. 6 *In-vitro* drug release profile of dapsone nanosponge.

Evaluation of Dapsone nanosponeged gel.

Physicochemical properties

Evaluation parameters	Results
Appearance	Shiny transperant
Viscosity (cps)	1245±0.75
Spreadability (g.cm/sec)	4
pH	6.4
Extrudability	+++
% Drug content	90.25±0.47

('+++' Excellent, '++' Better, '+' Good)

Table No. 3: Physicochemical properties of nanosponged gel.

***In-vitro* drug diffusion study**

SL. No.	Time in hours	% Cumulative drug release
1	0	0
2	1	12.64
3	2	20.80
4	3	32.46
5	4	43.60
6	5	55.86
7	6	66.20
8	7	78.80
9	8	89.30
10	12	96.60

Table no: - 04

- ***In-vitro* drug release kinetics**

Figure No. 7 Zero order kinetics

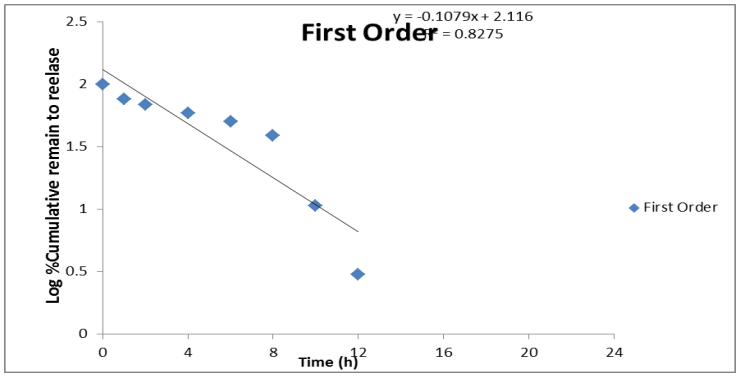

Figure No.8 First order kinetics

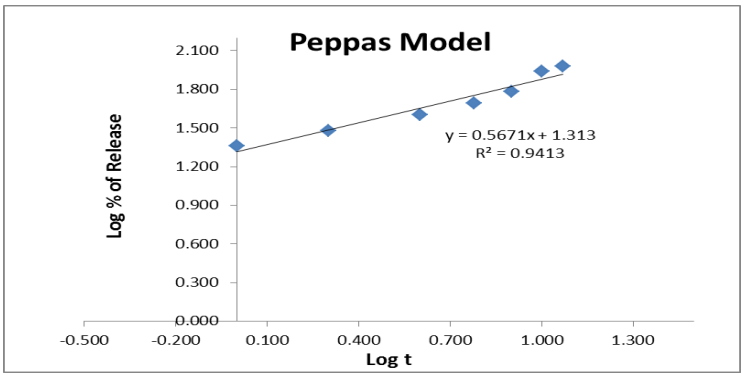

Figure No. 9 Peppas model drug release kinetics

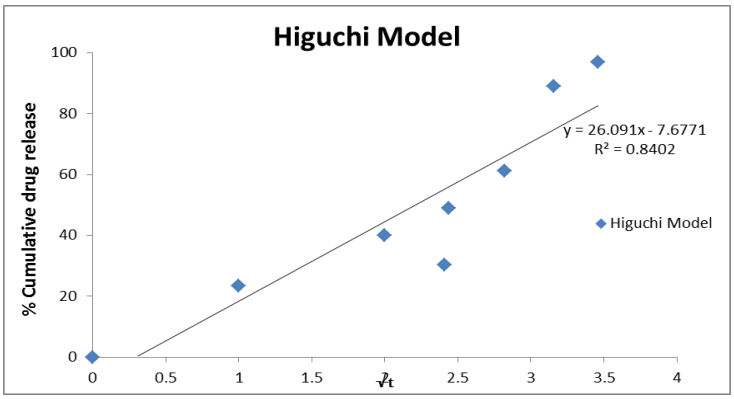

Figure No. 10 Higuchis model drug release kinetics

RELEASE KINETICS DATA

Formulation	Zero order	First order	Higuchi plot	Peppa's plot	
	R^2	R^2	R^2	R^2	N
Gel	0.9459	0.9367	0.9314	0.9829	0.8954

Table no: - 05 Release kinetics Data

Stability study

- **Drug content**

Evaluation parameters	**Time(days) (Accelerated conditions at 40±2˚C & 75±5% RH)**		
	0	30	60
Drug content	90.85±0.05	89.67±0.0.5	90.67±0.05

Table No: - 06 Drug content in stability studies.

DISCUSSION:

The aim of the study was to formulate and evaluate Dapsone nanosponge topical gel, The dapsone nanosponge were prepared by emulsion solvent diffusion method using different concentration of ethyl cellulose and polyvinyl alcohol. And the prepared nanosponges equivalent to 10% of Dapsone were loaded into the carbapol 934P gel.

PREFORMULATION STUDIES OF DRUG

a. Organoleptic charecterstics:

Organoleptic evaluation like general description colour, odour and taste of Dapsone were evaluated. It was found that Dapsone is odourless creamy white crystalline powder. The results obtained were shown in Table No.1

b. Solubility:

Literatures on solubility profile of dapsone indicates that drug is soluble in 7.2 pH phosphate buffer and slightly soluble in water. The study was carried out to select medium for the *in-vitro* drug release studies. The results obtained were shown in Table No. 1.

c. Melting point:

The study was carried out and found that the drug melted at 175°C temperature and results were shown in the Table No. 1

d. Determination of λmax:

The sample containing Dapsone was scanned in the range of 200-400nm by UV spectrophotometer against 7.2 pH phosphate buffer as blank. From the obtained spectrum absorbance maxima of the Dapsone was found to be at 293nm. This was accordance with reported values, the results are shown in Figure No.2 The same wavelength was used for further analysis.

e. Standard calibration curve of Dapsone:

Standard curve was prepared at the concentration of 2µg/ml to 10µg/ml in 7.2 pH PBS which gave a linear value of slope and R^2 as 0.102 and 0.994 respectively in wavelength of 293nm. The results were shown in Figure No. 3.

f. Compatibility study:

The IR spectra of drug loaded nanosponge formulation was compared with the standard spectrum of pure drug Dapsone, the characteristic peaks associated with specific functional groups and bond of the molecule and their presence/absence were noted in Table No. 6 and the overlay of pure drug and formulation was shown in the Figure No. 4 and 5.

Evaluation of Dapsone nanosponeged gel

a. Physicochemical properties:

The prepared gel containing nanosponge (F5) was evaluated for the physicochemical properties such as pH, readability, extrudability, Viscosity, and the drug content. Obtained data tabulated in Table. No.3 the values indicates that formulation showed good physicochemical properties.

b. *In-vitro* drug diffusion study:

The in-vitro drug diffusion of gel containing nanosponge were observed by dialysis method, the results obtained were shown in Table No. 4 and %CDR was found to be 96.60 at the end of 12hrs.

c. *In-vitro* drug release kinetics

The nanosponged gel formulation followed zero-order kinetics and their R^2 value was found to be 0.9459 indicating drug release is independent of initial concentration.

The N value for the korsmeyer-peppas for nanosponge gel was found to be 0.8954 so it follows non-Fickian type mechanism.

The drug release pattern of dapsone nanosponge gel follows zero order release and Non-Fickian diffusion mechanism as shown in Figure No. 7, 8, 9, & 10.

d. Stability studies

The results of the stability studies indicates that the nanosponge gel did not show any changes in the drug content and pH during stability study period.

The percentage cumulative drug release after 60 days showed 96.02% at the end of 12hrs. indicating no significant changes and the results obtained were depicted in Table No. 5 and 6.

CONCLUSION:

The precent study has been a satisfactory attempt to formulate nanosponge for controlled release topical delivery of Dapsone using ethyl cellolose as polymer, polyvinyl alcohol as surfactant and dichloromethane as crosslinking agent.

The following conclusions were drawn from the present study

- Preformulation studies of Dapsone comply with the reported literature limits.
- The IR spectra revealed that, there was no interaction between dapsone and polymer, thus indicating the compatibility of drug and polymers used.
- The Dapsone nanosponge were prepared by emulsion solvent diffusion method, the nanosponges were evaluated for percentage yield, drug entrapment efficiency, surface morphology, particle size and *in-vitro* drug release studies. Based on the results obtained from these parameters F5 formulation is considered as best with highest %CDR of 96.80 at the end of 12hrs.
- Nanosponges of formulation F5 were incorporated into gel and evaluated for p H, viscosity, spreadability, extrudability, drug

content, drug diffusion study, release kinetics and stability study.

- The %CDR of gel was found to be 96.60% at the end of 12hrs. formulation displayed zero order kinetics and drug release follows non-fickian diffusion mechanism.
- The stability studies were carried out for the gel, the results of drug content and in-vitro drug release studies showed no significant changes and indicates the good stability.

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