Development and Evalution of Different Platforms for the Treatment of Diabetic Wounds

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Abstract- Nanotechnology is defined as the manipulation of matter on an atomic, molecular, and supramolecular scale and involves the design, production, characterization, and application of various nanoscale materials in various potential areas, primarily in the field of medicine, to provide novel technological advancements. Nanosponges are extremely small mesh-like structures with an average diameter of less than 1 m. The medicine to be encapsulated and the required release determine the polymer to be used. The chosen polymer should be able to bind to particular ligands. Dapagliflozin will be more effective for a given dosage since it can be released at the precise target spot rather than spreading throughout the body. The primary goal of this research was to create Dapagliflozin -loaded Nanosponges formulation with reduced side effects while also reducing dosing frequency and dose.

Keywords: Nanotechnology, Nanosponges, polymer, Dapagliflozin.

INTRODUCTION

Nanotechnology is defined as the manipulation of matter on an atomic, molecular, and supramolecular scale and involves the design, production, characterization, and application of various nanoscale materials in various potential areas, primarily in the field of medicine, to provide novel technological advancements. Numerous medical specialties, including immunology, cardiology, endocrinology, ophthalmology, cancer, pulmonology, etc., may be affected by nanotechnology. Additionally, it is extensively used in specialist fields like gene delivery, tumour targeting, and brain targeting. Systems, tools, and materials made possible by nanotechnology are also important for improving pharmaceutical applications(1). Nanoparticles can be used for a wide range of things, including biocompatible materials, textile fictionalisation, UV protection coatings, medication delivery, DNA delivery, enzyme immobilisation, and more(2). There are many different types of nanoparticles, including micellar systems, dendrimers, solid lipid nanoparticles, carbon nanotubes, nanoemulsions, nanosponges, and polymeric nanoparticles. Nanotechnology has dominated technology since the 1950s(3). Nanoparticles can be divided into three categories based on how they interact with medications.

1) Encapsulating Nanoparticles: Nanosponges and nanosponges are examples of this class. Alginate nanosponges are sponge-like nanoparticles with several holes within that transport medicinal molecules. Nanoparticles are also being encapsulated by nanomaterials like poly (isobutyl cyanoacrylate, or IBCA). They have an aqueous core where drug molecules can be trapped.

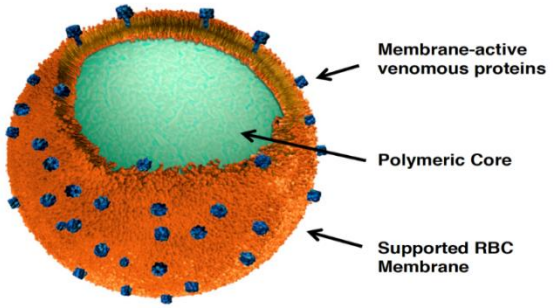
2) Complexing Nanoparticles: These particles attract molecules by electrostatic charges and fall under the category of complexing nanoparticles.)

3)Conjugating Nanoparticles: These nanoparticles form covalent bonds with medications to bind to them(4).

NANOSPONGES

The size of a virus, nanosponges are extremely small mesh-like structures with an average diameter of less than 1 m. These microscopic sponges can move through the body until they reach the intended target spot, where they adhere to the surface and start to release the medication in a steady, controlled manner. The drug will be more effective for a given dosage since it can be released at the precise target spot rather than spreading throughout the body(5). Three-dimensional networks or scaffolds are known as nanosponges. Scaffolds are often made of polymers and other substances that have been utilised for decades in drug delivery systems. Clinically significant functions can be added to scaffolds that

have extra drug delivery properties thanks to the combined efforts of medical professionals and material scientists[6]. They can improve the bioavailability of poorly soluble medications by binding them within the matrix due to their tiny size and porous structure[7]. They do this by altering the pharmacokinetic characteristics of the active ingredients.



(Figure no.1) Nanosponges

Characteristic Features of Nanosponges:

1. The tunable polarity of the cavities along with a variety of dimensions (1 m or less) is provided by nanosponges.
2. By altering the crosslinker to polymer ratio, nanosponges of a particular size can be created.
3. Depending on the circumstances of the processing, they either take on paracrystalline or crystalline forms. During the complexation of medicines, nanosponges' crystalstructure is extremely important.
4. Drug loading capacity varies with crystallisation level.
5. They can withstand pH levels between 1 and 11.
6. In water, they create an opalescent suspension that is transparent.
7. They are reproducible by straightforward thermal desorption, solvent extraction, microwave, and ultrasound technology.
8. Magnetic characteristics can also be added to nanosponges by including magnetic particles into the reaction mixture.
9. Nanosponges are highly soluble in water porous particles that are primarily utilised to encapsulate poorly soluble medicines.
10. These Nanosponges may transport both hydrophilic and lipophilic medications [7-9].

Composition of Nanosponges Polymer:

The performance and creation of Nano sponges can be affected by the polymer choice. The cavity size needs to be appropriate for incorporating the specific medication molecule. The medicine to be encapsulated and the required release determine the polymer to be used. The chosen polymer should be able to bind to particular ligands. Diphenyl carbonate, dichloromethane, dialyl carbonates, and diisocyanates are a few of the various examples [10].

- Drug molecules have a molecular weight of between 100 and 400 daltons and have fewer than five condensed rings.
- Solubility is less than 10 mg/ml in water.
- The substance's melting point is lower than 250 °C.

METHOD OF PREPARATION

1. Solvent method:

Mix the polymer with an appropriate solvent, preferably one that is polar and aprotic, like dimethylformamide or dimethyl sulfoxide. The extra crosslinker is then added to this mixture, preferably with a crosslinker/polymer molar ratio of 4 to 16. Perform the reaction for 1 to 48 hours at a temperature range from 100C to the solvent's reflux temperature. Allow the solution to cool at room temperature when the reaction is finished. Add the result to a large amount of distilled water, recover it by filtration under vacuum, and then purify it using a prolonged Soxhlet apparatus.

2. Emulsion solvent diffusion method:

Different ethyl cellulose and polyvinyl alcohol concentrations can be used to make nanosponges. To enhance drug loading and achieve a customised release, different drug to polymer ratios is utilised. A specific amount of polyvinyl alcohol in 100 ml of an aqueous external phase was added gradually over the course of three to five hours while stirring at a speed of 1000 to 1500 rpm using a magnetic or mechanical stirrer to dissolve the medication and polymer in the dispersion phase. The created nanosponges were collected by filtering, dried for 24 hours at 40 degrees Celsius, and then packaged.

3. Nanosponges made from hyper cross-linked β-cyclodextrins:

Materials used to create cyclodextrins, non-porous molecules used as carriers for drug release, are used to

create nanosponges. These cyclodextrins are hyper-cross-linking substances that create several nanoscale networks or can even take the form of a sphere with numerous networks of protein channels, pores, and other structures. Based on the chemicals they contain, these cross linkers stabilise the sponge with a particular surface charge density, porosity, and pore size. Cross linkers aid in maintaining Nano sponges at various acidic and even neutral pH levels[11].

4. Ultrasound-Assisted synthesis:

In this process, cross-linkers and polymers interact while being sonicated and without the use of a solvent. Here, combine the cross-linker and polymer in a flask. Heat the flask to 900 c and sonicate it for 5 hours in an ultrasound bath filled with water. After letting it cool, wash it with water to get rid of the unreacted polymer. Purify using an extended ethanol Soxhlet extraction. Vacuum-dry the product before storing it at 250°C.

5. Quasi-emulsion solvent diffusion:

The varied polymer quantities can also be used to prepare the nanosponges utilising the quasi-emulsion solvent diffusion approach. Eudragit RS100 was dissolved in a suitable solvent to prepare the inner phase.

Once a medicine has been introduced, the solution can be ultrasonically heated to 350 c to dissolve it. The inner phase was added to the water-based PVA solution (the outer phase) and stirred for one hour before filtering the mixture to remove the nanosponges. The nanosponges are dried for 12 hours in an air-heated oven at 40 °C.

6. Polymerization:

Aqueous phase, typically comprising surfactant and dispersant to enhance suspension, is added to a non-polar drug solution created in the monomer. Once the suspension with the distinct droplets of the correct size is established, polymerization is accomplished by catalysing or raising the temperature to activate the monomers

Loading of Drugs into Nanosponges:

The goal of pre-treating nanosponges for drug delivery is to achieve a mean particle size of less than 500 nm. To avoid the formation of aggregates, sonicate the nanosponges in water, then centrifuge the suspension to separate out the colloidal fraction. Prepare the Nanosponge aqueous suspension, disperse any extra medication, and keep the suspension constantly stirred for the precise amount of time needed for complexation. Then, by solvent evaporation or freeze drying, produce the solid nanosponges crystals[12].

METHOD OF PREPARATION

The process used to load the medicine into the nanosponge can influence how the drug and nanosponge interact. Freeze drying has been proven to be the most effective approach for drug complexation in many circumstances, albeit the efficiency of a method depends on the nature of the drug and polymer. The kind, number, and position of the substituents on the parent molecule may have a significant impact on the degree of substitution as well as the nanosponge's capacity for complexation [13]

MATERIALS AND METHODS

The instruments and chemicals used that are AR Grade or the best possible pharma grade available were used for the experimental studies.

Table No: 1The list of drugs and excipient, their manufacturer and role in the present study.

EQUIPMENTS USED FOR PREPRATION OF NANOSPONGES

NAME OF THE EQUIPMENT	MANUFACTURER/ SUPPLIER
Electronic balance	Asha scientific company,Mumbai
High speed homogenisor	Remi electrotechnic,Vasai
Hot air oven	Mc dalal, Chennai
Optical microscope	Sigma Scientific Instrumentation, Chennai
pH meter	Mc dalal, Chennai
Dissolution apparatus	Campbell electronics, Mumbai
UV spectrophotometer	Shimadzu,Japan
FT-IR spectrophotometer	Shimadzu, Japan
SEM Analyser	Hitachi, Japan

(Table No: 1) Equipment used in the formulation and evaluation of Nanosponges

EXPERIMENTAL STUDIES

Preparation of phosphate buffer (pH7.4)

An accurately weighed quantity of 28.80gm of disodium hydrogen phosphate and 11.45gm of potassium dihydrogen phosphate was dissolved in sufficient water to produce 1000ml.

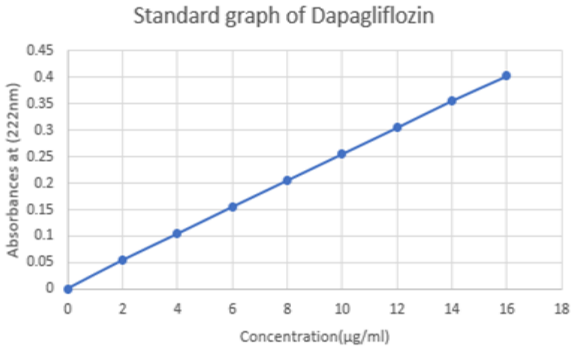
Calibration of standard curve of Dapagliflozin:

For the quantitative estimation of dapagliflozin, a spectrophotometric approach that has been slightly

changed has been established. By dissolving 10 mg of dapagliflozin in enough amounts of ethanol and making up the difference with ethanol, a stock solution of dapagliflozin was created. From there, 10 ml was pipetted into a standard flask of the same size, and the required amount of phosphate buffer pH 7.4 solution was added. From this, pipets were used to separate out aliquots of 2 ml, 4 ml, 6 ml, 8 ml, 10 ml, 12 ml, 14 ml, and 16 mcg/ml (equal to 2, 4, 6, 8, 10, 12, 14, and 16 mcg/ml) and produce up to 10 ml with phosphate buffer pH 7.4 solution. The absorbance of the solution was determined in UV-Visible spectrophotometer at 222 nm using phosphate buffer pH7.4 as blank.A standard curve was drawn by relating concentration (µg/ml) on X-axis and absorbance of dapagliflozin at 222nm on Y-axis.

(Table NO: 2)Absorbance of dapagliflozin in phosphate buffer pH-7.4

SNO	CONCENTRATION (µg/ml)	ABSORBANCE (222nm)
1	2	0.054
2	4	0.104
3	6	0.155
4	8	0.205
5	10	0.255
6	12	0.305
7	14	0.356
8	16	0.403



(Figureno.2)Standard graph of Dapagliflozin in phosphate buffer pH-7.4

Preparation and optimization of nanosponges containing dapagliflozin:
Dapagliflozin nanosponges were prepared by using emulsion solvent diffusion method with two polymers with different ratios.

(Table:No: 3) Composition of Dapagliflozin Nanosponges

INGREDIENTS	F-1	F-2	F-3	F-4	F-5	F-6
Dapagliflozin(mg)	10	10	10	10	10	10
HPMC E5	1:1	1:2	1:3	-	-	-
HPMC E15	-	-	-	1:1	1:2	1:3
Polyvinyl alcohol(mg)	0.153	0.153	0.153	0.153	0.153	0.153
Dichloromethane(ml)	3	3	3	3	3	3
Distilled water(ml)	30	30	30	30	30	30

Procedure to formulate nanosponges: Different ratios of HPMC E15, polyvinyl alcohol, and HPMC E5 were used in the emulsion solvent diffusion technique to create dapagliflozin-loaded nanosponges. A specific amount of PVA in 30 mL of an aqueous continuous phase was added gradually after the organic phase, which contained 10 mg of dapagliflozin and a specified amount of HPMC E5 and HPMC E15 dissolved in 3 mL of dichloromethane, was added. The mixture was agitated for two hours at a speed of 1000 rpm on a magnetic stirrer. The resulting nanosponges were then collected by vacuum filtration and dried for twenty-four hours at 40 °C.

PREFORMULATION STUDIES OF DRUG

Preformulation studies are usually provide a tool to select suitable excipients compatible with selected drugs and play a key role for development of new formulation.it is the first step in development of a drug substances.it gives the information needed to define the nature of the drug substance and provide a framework for the obtained sample of the drug for identification
and compatibility .

- ✓ Organoleptic properties
- ✓ Solubility analysis
- ✓ Melting point determination
- ✓ Compatibility studies
- ✓ Fourier transform infrared spectroscopy

Organoleptic properties

The organoleptic characters of the drug like color, odour, taste and appearance play an important role in the identification of the sample and hence they were recorded in a descriptive terminology.

Solubility analysis

The amount of substance that passes into solution in Order to establish equilibrium at constant temperature and pressure to produce a saturated solution is known as solubility. Solubility analysis was carried out to find an appropriate solvent to dissolve the drug and to test the solubility for the dissolution medium used [14].

Melting point determination:

The pharmacopeias regard the capillary method as the standard technique for melting point determination.in this methodology, a thin glass capillary tube containing a compact column of the substance to be determined is introduced into a heated stand (liquid bath or metal block) in close proximity to a high accuracy thermometer. The temperature in the heating stand is ramped at a user-programmable fixed rate until the sample in the tube transitions into the liquid state. While determining a melting point, several observations and the temperature are recorded.

Compatibility studies:

Infrared spectroscopy was conducted using FT-IR spectrophotometer and the spectrum was recorded in the wave number region of 4000 to 400 cm^{-1}. The procedure consisted of dispersion the sample (drug alone, mixture of drug and excipients and the optimized formulation) in potassium bromide and compressed into disc by applying a pressure of 5 tons for 5 minutes in a hydraulic press. The pellet was placed in the light path and the spectrum was recorded [15].

EVALUATION OF NANOSPONGES

PRODUCTION YIELD:

Presentage yield can be determined by calculating the initial weight of raw materials and the finally obtained weight of nanosponges. Percentage yield can be calculated by using the formula:

$$\text{Production yield} = \frac{\text{Theoretical yield}}{\text{Practical yield}} \times 100$$

LONDING EFFICIENCY:

The nanosponges was determined spectrophotometrically (max = 340 nm). A sample of dapagliflozinnanosponges (100 mg) was dissolved dissolved in 100 ml of phosphate buffer (pH-7.4) and kept for overnight. The drug content was determined and expressed as actual drug content in nanosponge. The loading efficiency (%) of the nanosponges was calculated according to the following equation [16].

$$\text{Loading Efficiency} = \frac{\text{Actual drug content in nanosponges}}{\text{Theoretical Drug content}} \times 100$$

SURFACE MORPHOLOGY:

Scanning Electron Microscopy of optimized nanosponge formulation was carried to determine the surface morphology. The sample was mounted directly onto the SEM sample holder using double sided sticking tape and images were recorded at different magnifications at acceleration voltage of 10 kV using scanning electron microscope.

IN-VITRO DRUG RELEASE STUDY:

In-vitro release rate studies of nanosponges were carried out by filling equivalent amount of nanosponges in nanospongess placed in the basket containing phosphate buffer pH 7.4 was used as medium and rotated at 50 rpm. Samples was withdrawnand determined by spectrophotometrically at 222 nm [17].

BULK DENSITY:

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below.It is expressed in g/ml and is given by $\rho_b = M/V_b$

Where, M and V_b are mass of powder and bulk volume of the powder respectively.

TAPPEDDENSITY:

It is the ratio of weight of the powder to the tapped volume of powder. The powder was introduced into a measuring cylinder with the aid of funnel and tapped for 500 times on a wooden surface at a 2 sec interval and the volume attained is the tapped volume.

ρ_t=M/V_t

Where, M and V_t, are mass and tapped volume of the powder respectively.

It is expressed in g/ml.

ANGLE OF REPOSE:

The flow properties were characterized in terms of angle of repose, Carr's index and hausner's ratio. For determination of angle of repose (θ) the drug and the blend were poured through the walls of the funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above hard surface. The drug or the blends were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. Angle of repose was calculated using following equation.

$$\theta = tan^{-1}(h/r)$$

Where, h=height of the pile in cm and r= radius of the pile in cm.

CARR'S INDEX:

It indicated powder flow properties, it is measured for determining the relative importance of inter particulate interactions. It is expressed in percentage and is given by

$$CI=\frac{\rho t-\rho b}{\rho t} \times 100$$

Where and are tapped density and bulk density respectively.

FLOW PROPERTY	ANGLEOF REPOSE(θ)	COMPRESSIBILITY INDEX (%)	HAUSNER'S RATIO
Excellent	25-30	<10	1.000-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very poor	56-65	32-37	1.46-1.59
Very poor	>65	>38	>1.60

(TableNo:4) Angle of Repose, Compressibility Index and Hausner'sRatio

RESULT AND DISCUSSION

PREFORMULATION STUDIES

The present study wasundertaken to formulate controlled release Dapagliflozin nanosponge using two polymers (HPMC E5&HPMC E15) with three different ratios and prepared by emulsion solvent diffusion method. Before preparation of the evaluation studies such as bulk density, tapped density, angle of repose, Carr's index, and hausner ratio were determined and tabulated in the table after that evaluation tests of nanosponges such as percentage yield, loading yield, loading efficiency, particle size distribution and other parameters such as in vitro drug release, IR analysis studies and solubility studies were also performed and the results are presented.

OROGANOLEPTIC CHARACTER

The result was shown on table no: 5

PROPERTIES	RESULTS
Color	White or off-white
Odor	Odourless
Taste	Slightly bitter
Appearance	Powder

(Table no:5) Organoleptic character

SOLUBILITY

Solubility test for Dapagliflozin was carried out in different solvents such as ethanol, water, dichloromethane and chloroform and results are given in Table 6.

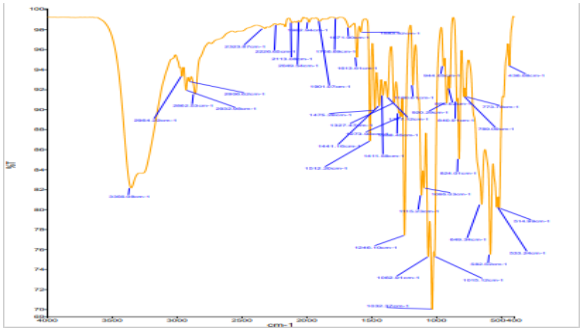
SL.NO	SOLVENT	DESCRIPTION
1.	Water	Freely Soluble
2.	Ethanol	Soluble
3.	Dichloromethane	Soluble
4.	Chloroform	Slightly soluble

(Table no.6) Solubility test for Dapagliflozin for Different Solvents.

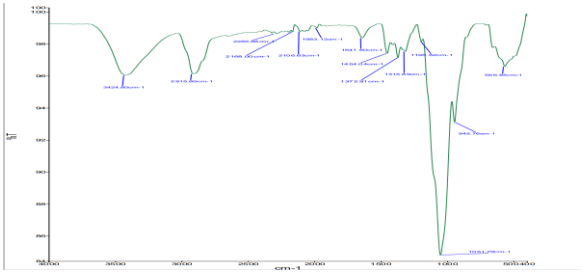
FOURIER TRANSFORM INFRA RED SPECTROSCOPY (FTIR) STUDIES REPORTS:

The FT-IR infrared spectroscopy was carried out separately to check the compatibility between drugs(Dapagliflozin) and the polymers(HPMC E-5,HPMC E15) used for the preparation of nanosponges. The FT-IR was preformed for pure drugs, polymers and physical mixture of drugs and polymers. The spectra studied at 4000cm^{-1} to 400cm^{-1} are shown in figures-8 it was found from the spectra that there were no major shifting as well as any loss of functional peaks in the spectra of drugs, polymers and physical mixture of drugs and polymers. The results

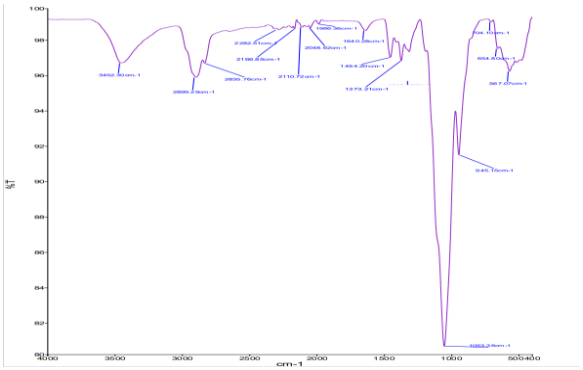
indicate that the selected polymers are found to be compatible with the selected drugs Dapagliflozin. Interaction between the drug and excipients used in the formulation was studied. The results are shown in figure no: 3-7.



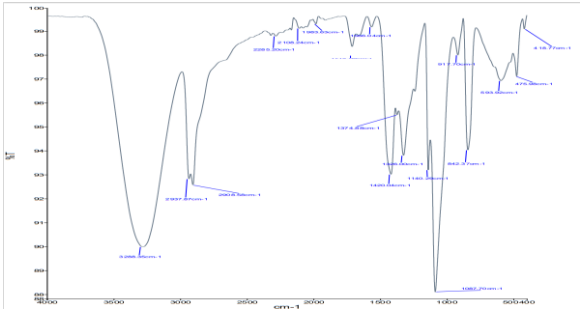
(Figure No: 3) FT-IR Spectrum of Pure Drug (Dapagliflozin)



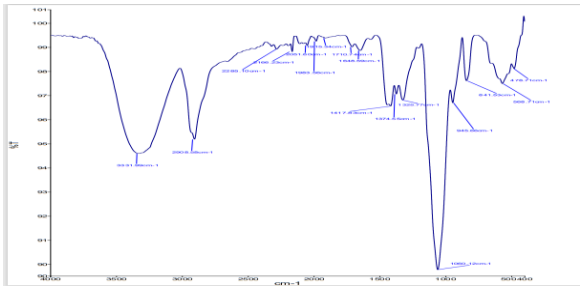
(Figure No: 4) FT-IR Spectrum of Polymer (HPMC E5)



(Figure No: 5) FT-IR Spectrum of Polymer (HPMC E15)



(Figure No: 6) FT-IR Spectrum of PolyVinylAlcholol



(Figure no: 7) FT-IR Spectrum of Drug Mixture

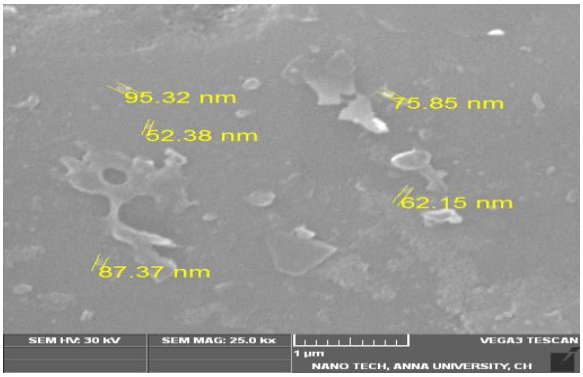
The FTIR interpretations indicated that there is no interactions observed in all formulations of nanosponges.

SCANNING ELECTRON MICROSCOPY (SEM):

SEM was used to investigate the morphology of nanoparticles. The SEM micrographs formulations - 2(Dapagliflozin with HPMC E5) and 3(Dapagliflozin and HPMC E15) are presented in figuresno.8

The SEM images showed that the surface of prepared nanosponges was smooth and spherical in shape and uniform in size and ideal surface morphology. It showed no aggregation due to the result of negative zeta potential on the surface of then nanoparticles that prevent the agglomeration process.

The images are shown in fig no: 8



(Figure No: 8) SEM Image of Dapagliflozin Nanosponges.

BULK DENSITY

The bulk density of all formulations was measured by using measuring cylinder. The bulk density was in the range of 0.25 gm/cm^3 -0.36gm/cm^3.It is within the acceptable limits. The result are shown in table.8

TAPPED DENSITY

The tapped density of all formulations was determined by using measuring cylinder. The tapped density was found in the range 0.444gm/cm^3 - 0.473 gm/cm^3. It

showed that the tapped density was within the acceptable limits. The result shown in table no.8

ANGLE OF REPOSE

The angle of repose of all formulations was found in the range of 32^0. If the angle of repose is within 35^0 it includes good flow property of the powder/granules. The result showed that the flow properties of all formulation are 31^0-35^0.The result are shown in table no.8

If the compressibility index of granules is between 11-15.it shows good flow character. Here all the formulations exist in the range 11-15. It indicates that the granules showed good flow character. The result shown in the table.8

HAUSNER'S RATIO

The result odhausner's ratio of all the formulation was between 1.12-1.18. If the Hausner's ratio lies between 1.12-1.18.it shows good flow behavior of the granules or powder. The result indicates the good flow property of the granules. The result are shown in table.

CARR'S INDEX

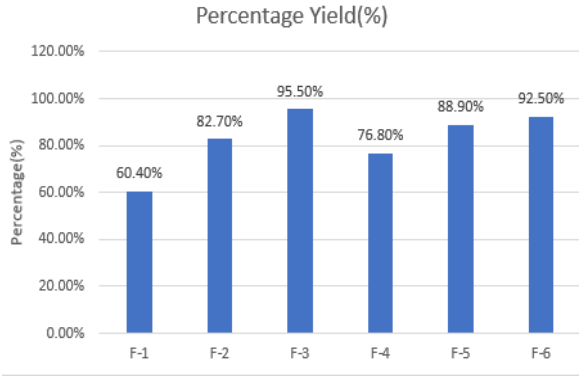
FORMULATION CODE	BULK DENSITY gm/cm^3	TAPPED DENSITY gm/cm^3	CARR'S INDEX (%)
F-1	0.25 ±1.5	0.445 ± 0.007	13.9 ±0.007
F-2	0.35± 0.11	0.474± 0.003	11.04± 4.36
F-3	0.27 ± 0.21	0.446± 0.01	11.28± 1.3
F-4	0.31 ± 0.05	0.444± 0.33	16.14± 2.5
F-5	0.34 ± 0.18	0.464± 0.21	21.01± 0.3
F-6	0.35±0.19	0.454±0.23	17.14±0.4

(Table no: 7) Preformulation Parameters of Drug Nansponges

Nanosponges The flow property of pure drug was found to be very poor. Good flow property was observed for.

EVALUATION OF NANOSPONGES:

FORMULATION CODE	THEORETICAL YEILD	PRACTICAL YIELD	PERCENTAGE YIELD(%)
F-1	0.777	0.470	60.4%
F-2	0.888	0.662	82.7%
F-3	1.2	1.14	95.5%
F-4	0.800	0.615	76.8%
F-5	1.0	0.889	88.9%
F-6	1.2	1.1	92.5%



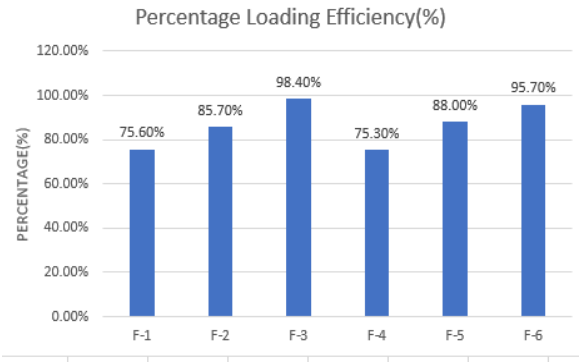
(Figure no: 9) Percentage Yield (%)

LOADING EFFICIENCY:

%Loading efficiency ranged from 75.3% to 98.4%. Highest loading efficiency was found for the formulation F-3 to F-6 this shows that the increasing drug: polymer ratio increased loading efficiency. The result corresponds to earlier reports. The results are shown in table no: 10&fig no 8.

(Table No:8) Percentage Loading Efficiency

Formulation Code	Loading Efficiency (%)
F-1	75.6%
F-2	85.7%
F-3	98.4%
F-4	75.3%
F-5	88.0%
F-6	95.7%



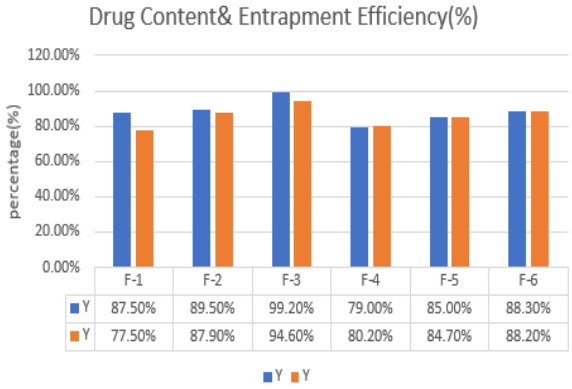
(Figure no: 10)Percentage Loading Efficiency (%)

DRUG CONTENT:

Drug Content and entrapment efficiency ranged from 79.0% to 99.2%. Highest entrapment efficiency and drug content was found for the formulation f-3 to f-6This shows that the increasing drug: polymer ratio increased drug content. The result corresponds to earlier reports. The result are shown in table no: 9&fig no 11.

FORMULATION CODE	DRUG CONTENT (%)	ENTRAPMENT EFFICIENCY (%)
F-1	87.5%	77.5%
F-2	89.5%	87.9%
F-3	99.2%	94.6%
F-4	79.0%	80.2%
F-5	85.0%	84.7%
F-6	88.3%	88.2%

(Table no: 9) Drug content and entrapment efficiency



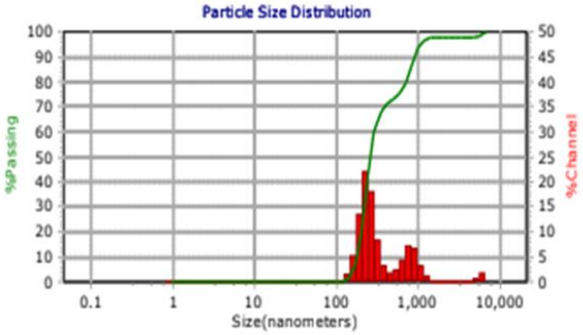
(Figure no: 11)Drug Content &Entrapment Efficiency (%)

PARTICLE SIZE DISTRIBUTION:

From the above results, it was found that particle size distribution was in the range of 283.9µmto384.0µm. This reveals as drug: polymer increases the particle size went on decreasing. The results corresponds to earlier reports. The result are shown in the table no: 10S & fig no: 12

S. NO	FORMULATION	AVERAGE PARTICLE SIZE (µm)	ZETA POTENTIAL
1	F-1	311	39.8 (+ve)
2	F-2	312.0	58.3 (+ve)
3	F-3	283.9	133.3 (-ve)
4	F-4	384.0	49.2 (-ve)
5	F-5	306.0	68.3 (-ve)
6	F-6	304.0	57.9 (-ve)

(Table No: 10) Average Particle Size of Nanosponges



Summary	
Data	Value
MI(nm):	500.0
MN(nm):	209.2
MA(nm):	283.9
CS:	21.14
SD:	285.0
PDI:	0.324
Mz:	407.7
σι:	0.2742
Ski:	0.778
Kg:	1.018

Percentiles	
%Tile	Size(nm
10.00	182.0
20.00	204.3
30.00	221.8
40.00	239.5
50.00	260.5
60.00	289.5
70.00	373.0
80.00	693.0
90.00	881.0
95.00	1035

(Figure No: 12) Particle Size Distribution

IN-VITRO DRUG RELEASE OF NANOSPONGES:

The dissolution character of dapagliflozin Nanosponges from controlled release Nanosponges was evaluated in vitro using two polymers in three ratios. Table 13 and Figure 13 show the results of all formulation's in-vitro release studies.

After 11 hours, the percentage drug release of all formulations using HPMC E5 AND HPMCE15 was found to be 79.2%. (Dapagliflozin: HPMC-E5). (1:1), 90.2%, (1:2), 94.4% (1:3), and (Dapagliflozin:HPMCE15), (1:1), 80.4%, (1:2), 82.6%, (1:3) 86.4%.

When comparing the percentage release of dapagliflozin from formulations F-3 containing dapagliflozin: HPMCE5 (1:3) and F-6 containing dapagliflozin: HPMC E15 (1:3), (1:3). This is consistent with previous reports. The percentage drug release of dapagliflozin increased as the polymer ratio was increased.

The polymer concentration had a significant impact on drug release.The drug release was greater at higher polymer concentrations than at lower polymer concentrations

SUMMARY AND CONCLUSION

Nanosponges are microscopic particles with a few nanometers wide cavities that can encapsulate a wide range of substances. These particles can transport both lipophilic and hydrophilic substances, improving the solubility of poorly water soluble molecules. Drugs encapsulated within the Nanosponges pores are protected from premature degradation, and drug stability is improved.

The primary goal of this research was to create Dapagliflozin-loaded Nanosponges using various polymers to target pancreatic cells and release the drug in a controlled manner. This formulation reduced side effects while also reducing dosing frequency and dose.

The current study used an emulsion solvent diffusion method to create Dapagliflozin nanosponges from two different types of hydrophobic polymers (HPMC E5&HPMC E15).

This method was simple and inexpensive.

Dapagliflozin's solubility was determined through preformulation studies. A solubility test revealed that Dapagliflozin is not water soluble but is soluble in solvents such as ethanol, dichloromethane, and others.

The FTIR and UV spectral studies validate the spectra obtained with the sample drug when compared to the standard pure drug. The maximum absorption peak was found in UV spectra at 222nm.

The comparison of the FTIR spectra of Dapagliflozin and the mixture of Dapagliflozin and polymer confirms the absence of new peaks and the disappearance of existing peaks from the drug. This indicates that no interaction exists between the drug and the polymer used in the study.

The emulsion solvent diffusion method was used for formulation. Hydrophilic polymers were found to be unsuitable for Dapagliflozin nanosponges in trial batches. The hydrophilic polymers yielded no or very little yield. Hydrophobic polymers resulted in effective formulations. HPMC E15 and HPMC E5 were chosen for further research.

SEM images of the prepared nanosponges at various magnifications revealed that they were porous with a smooth surface morphology and spherical shape. The SEM images clearly show the spongy and porous nature of nanosponges.

The Malvern Zeta sizer was used to determine particle size and zeta potential. The prepared sample's particle size was confirmed by particle size analysis to be in the nanometer range. The average particle size obtained for formulations F-3 and F-4 was 283.9nm and 384.0nm, respectively. The zeta potential values of the nanosponges indicated that the nanosponges were stable.

The amount of drug entrapped in nanosponges was calculated, and all of the prepared nanosponges had extremely high entrapment efficiency.

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