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FORMULATION AND CHARACTERIZATION OF NANOSPONGE-LOADED GEL OF EXTRACTED FUCOIDAN FROM *DICTYOTA BARTAYRESIANA* FOR ANTI-ARTHRITIC ACTIVITY

Pavithra Sugumar, Mythili Krishnamurthy * and Praveen Kumar Sankar Umapathy

Sri Ramachandra Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai - 600116, Tamil Nadu, India.

Keywords:

Dictyota bartayresiana, Fucoidan, Anti-arthritic activity, Nanosponge loaded gel

Correspondence to Author:
Dr. Mythili Krishnamurthy

Associate Professor,
Sri Ramachandra Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai - 600116, Tamil Nadu, India.

E-mail: pharmaceuticalqa2021@gmail.com

ABSTRACT: The study aimed to develop a novel gel loaded with nanosponges containing fucoidan extracted from *Dictyota bartayresiana* for arthritis treatment. Brown algae are rich in fucan, a group of sulfated polysaccharides with superior healing properties. Among the numerous fucoidan sources, a species, *Dictyota bartayresiana*, was selected from the family Dictyotaceae for arthritis screening. Many types of arthritis are characterized by inflammation, stiffness, redness, and pain. The protein denaturation method was used for the in vitro anti-arthritic study of ethanolic extract of *Dictyota bartayresiana*. Percentage inhibition of five series of concentrations ranging from 100 - 1000 µg/ml of test solution showed values of 51.86% w/w, 55.56% w/w, 59.26% w/w, 65.19% w/w, and 85.49% w/w concerning with the standard, respectively. A concentration of 1000 g/ml induced an effective percentage inhibition. Fucoidan's beneficial properties guide the development of effective formulations. Fucoidan isolated from algae is formulated in the form of nanosponges using an emulsion solvent diffusion method and developed in gel-loaded nanosponges with the help of carbopol 940 polymer. Because of the nanosize of the particles, topical gel formulations embedded with nanosponges are non-toxic, flexible and useful methods of controlling drug release pattern and penetration through the skin. *In-vitro* release kinetics data were analyzed to determine possible release kinetics order and mechanism. A nanosponge-loaded gel of extracted fucoidan exhibits a zero-order profile and provides sustained release of the compound.

INTRODUCTION: Seaweeds are important anticipated marine resources that are considered remedies for various areas of food, cosmetics, pharmaceuticals, nutraceuticals and biotechnological industries.

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The principal constituents of fucoidan, alginate, agar and carrageenan are influential pharmaceuticals [1]. The availability of the major constituents varies by seaweed colour and geography.

Apart from fucoidan, various ingredients such as alginates and laminarian are also present in brown algae, which are equally important in the pharmaceutical field [1]. Defensive activities of fucoidan from marine brown algae approached for arthritic study [2]. Most members of the genus *Dictyota* reported cytotoxic and anti-viral

activity. Fucoidan extracted from the resource *Dictyota bartayresiana* reported cytotoxic, anti-bacterial [3], anti-cancer [4] and anti-fungal activity [5]. This stimulates the importance of screening *Dictyota bartayresiana* for anti-arthritic study. Marine polysaccharides-based nanomaterials are excellent candidates for cancer immuno-therapies and biomedical fields [6]. They are stable, biocompatible, biodegradable, and non-toxic. Sulphated polysaccharides, particularly fucoidans have been incorporated in nanosystems for analytical, drug delivery, regenerative medicine, and tissue engineering for theranostic applications [7].

Fucoidans have also been used as stabilizers of nanoparticles. The structure, composition, and yield of fucoidan depend on its extraction process. It was reported that the composition of fucoidan varies with different sources of brown algae, such that the extracted fucoidan from *Fucus vesiculosus* has rich content of fucose and sulphate whereas fucoidan extracted from *Sargassum stenophyllum* has high content of residues (galactose, mannose, glucose, xylose and glucuronic acid) than fucose and sulphate content. Fucoidan's bioactivity is dependent on its molecular weight, algae Source, the harvest season, and the extraction method [8].

The novel drug delivery system has arisen with an enormous targeted drug delivery which has a well-known result on the affected site. The beneficial value of the drug depends on the concentration, penetration of the drug across the membrane barriers, and accessibility of fucoidan at the exact affected part. Among the current formulation research and development, nanosponges were established to be emerging drug delivery systems based upon their loading capacity, prolonged and controlled drug release, and effective therapeutic activities [9].

Nanosponges are characterized as nanoparticles consisting of cavities with wide space that act as carrier molecule. Nanosponges (NS) are new colloidal constitutions derived from a new class of hyper-crosslinked polymers and include solid colloidal nanoparticles with nanosized cavities. NS has three-dimensional complexes with a lengthy polyester backbone. The polymer in solution form is combined with a small molecule, cross-linker, which acts like minute seizing locks to collectively hold dissimilar parts of the polymer, thereby forming approximately sphere-shaped particles with cavities to accumulate the drug molecules in it [10]. Fucoidan is suitable for oral administration but has an obstructed permeability through intestinal epithelial cells and low oral bioavailability because of its molecular weight. Fucose-rich poly-saccharides elicited a rational drug delivery strategy with less accumulation in the plasma when applied topically to inflammatory skin conditions [11].

MATERIALS AND METHODS:

Collection and Authentication: *Dictyota bartayresiana* was collected in the month of July 2019 and authenticated by R. K. Algae project center, Thoonithurai, Mandapam, Ramanathapuram district, Tamilnadu.

Extraction of Fucoidan: The milled sample was added with 99.9 %v/v ethanol in the ratio (1:2). The mixture was stirred for 1 hour to remove proteins and pigments and centrifuged for 10 min. The precipitate was collected, mixed with double distilled water (1:10), and kept in a water bath for 10 min at 40ºc with continuous shaking. The mixture was centrifuged at 2000 RPM for 10 min and the supernatant was collected.

The collected supernatant was added with ethanol (99.9 % v/v) to get a final ethanol concentration of (20 % v/v). The supernatant was collected, and 99.9% v/v ethanol was added until a final ethanol concentration of 50% v/v was reached in order to get fucoidan precipitate. The precipitated fucoidan was then collected by centrifugation at 3000 RPM for 30 mins and dried at 40º C. The precipitated fucoidan was collected by centrifugation technique and calculated for its yield[12].

Percentage yield = Practical yield / Weight of the sample taken × 100

Phytochemical Screening: To determine its purity, Fucoidan from *Dictyota bartayresiana* was subjected to phytochemical screening in triplicate. The tests included alkaloids, carbohydrates, flavonoids, steroids, saponins, and tannins. A sulfate confirmation test was conducted to confirm the sulfate content in the seaweed.

Characterization of Fucoidan by Spectroscopic Analyses:

UV-Visible Spectrophotometric Method: The standard fucoidan was accurately weighed and dissolved to achieve the concentrations of 5, 10, 15, 20, and 25 µg/ml. The standard solutions were scanned in a UV-visible spectro-photometer (Shimadzu UV 1800). The absorbance of fucoidan was measured at 202 nm.

FT-IR Study: A Perkin-Elmer (4100 JASCO) Fourier Transform Infrared (FT-IR) spectrometer was used to analyze fucoidan qualitatively. Fucoidan was scanned in the mid-infrared region (4000-400 cm^{-1}). An interpretation of the results from the identification of functional groups in sulphated polysaccharides was provided [13].

***In-vitro* Study of Anti-Arthritic Activity:**

Inhibition of Protein Denaturation Method: The sample solution (0.5 ml) consisted of 0.45 ml of bovine serum albumin and 0.05 ml of seaweed extract (ethanolic) at varying concentrations. The samples were incubated at 37º C for 30 min. Then it was permitted to be cooled, and 2.5 ml of freshly prepared phosphate buffer saline (pH 6.3) was put into each test tube, and the turbidity was computed spectrophotometrically at 660 nm. The test control and product control of 0.05 ml were prepared identically with minor differences such that the control test used distilled water instead of extracts while product control does not have bovine serum albumin. The percentage inhibition of protein denaturation was calculated. The control represents 100% denaturation. To interpret the results, standard solutions treated with Diclofenac sodium were compared to the sample solutions [14].

% Inhibition=100 - Optical density of test solution – Optical density of product control / Optical density of test control × 100

Formulation of Fucoidan Nanosponges: Fucoidan nanosponge was formulated by the emulsion solvent diffusion method. In the manufacturing process, two phases are prepared: an organic phase and an aqueous phase. The organic phase consists of fucoidan and ethyl cellulose, completely liquefied in dichloromethane (cross-linker). The aqueous phase consists entirely of polyvinyl alcohol (surfactant) dissolved in water with the aid of heat and constant stirring. The organic phase was then gradually incorporated into the aqueous phase by stirring with a magnetic stirrer at 1200 rpm for 2 h at room temperature. Nanosponges were filtered and dried using a hot air oven at 40ºC for 8 h and stored in a firmly closed container [15]. The formulation of fucoidan nanosponge is presented in **Table 1**. The percentage yield of fucoidan nanosponge was calculated by using the formula below:

Percentage yield (%) = Practical yield of nanosponge / Theoretical yield (drug + polymer) × 100

TABLE 1: FORMULATION OF FUCOIDAN NANOSPONGE

S. no.	Ingredients	F1	F2	F3	F4
1	Fucoidan(g)	1	1	1	1
2	Ethyl cellulose (g)	2	2.5	3	3.5
3	Polyvinyl alcohol (g)	3	3	3	3
4	Dichloromethane (ml)	20	20	20	20
5	Distilled water (ml)	100	100	100	100

Evaluation of Fucoidan Nanosponge:

Drug Entrapment Efficiency: Fucoidan nanosponges of different ratios (F1, F2, F3, and F4) were weighed and crushed in a mortar and pestle. Approximately 5 ml of ethanol was added and transferred to 100 ml standard flasks filled with Phosphate buffer solution (pH 7.4). The nanosponges are left aside for 1 h with repeated shaking to extract the drug. The absorbance was measured spectrophotometrically at 202 nm after filtering the solution [15]. The drug content was calculated from the calibration curve and expressed as actual drug content in nanosponge. The drug entrapment efficiency (%) of the nanosponge was calculated according to the formula:

Drug entrapment efficiency (%) = Initial weight of drug–free non-entrapped drug / Initial weight of drug x 100

Scanning Electron Microscope (SEM) Analysis: The investigation of the physical characteristics of particles is an essential part of drug product development. We examined particle size and shape of fucoidan nanosponge selected from various concentrations using scanning electron microscopy.

Formulation of Fucoidan Nanosponge Loaded Gel: An exact weighed amount of carbopol 940 with varying ratios was dissolved in water. This gel base was stirred under a magnetic stirrer to ensure homogeneity. The fucoidan nanosponges of the F1

formulation are homogeneously dispersed. As a permeation enhancer, propylene glycol was added. Preservatives such as methylparaben and propylparaben have been added. As a pH adjuster, triethanolamine was added slowly and constantly stirred until a gel consistency was reached [16]. The formulation of fucoidan nanosponge-loaded gel was presented in **Table 2.**

TABLE 2: FORMULATION OF FUCOIDAN NANOSPONGE LOADED GEL

S. no.	Ingredients	G1	G2	G3	G4
1	Carbopol (g)	0.5	1	1.5	2
2	Fucoidan (g)	1	1	1	1
3	Propylene glycol (ml)	2	2	2	2
4	Methyl paraben (0.5%)	0.02	0.02	0.02	0.02
5	Propyl paraben (0.2%)	0.002	0.002	0.002	0.002
6	Triethanolamine (ml)	Quantity sufficient	Quantity sufficient	Quantity sufficient	Quantity sufficient
7	Distilled water (ml)	Quantity sufficient	Quantity sufficient	Quantity sufficient	Quantity sufficient

Evaluation of Fucoidan Nanosponge Loaded Gel:

Physical Examination: The prepared fucoidan nanosponge-loaded gel was examined visually for colour, consistency, and homogeneity.

Determination of pH: A digital pH meter was used to measure the pH of the nanosponge-loaded gel formulations (G1, G2, G3, and G4). PH measurements were conducted in triplicate for each formulation, and average values were calculated.

Viscosity: The viscosities of various nanosponge-loaded gel formulations (G1, G2, G3, G4) have been determined using a Brookfield viscometer. Viscosity was determined using a spindle 18 and a rotational speed of 10 RPM for gel loaded with 1% w/v nanosponge [17].

Spreadability Study: A circle of 1 cm diameter was pre-marked on a ground glass slide with about 1 g of fucoidan nanosponge-loaded gel. The gel formulation was sandwiched between this slide and the second slide containing the gel formulation. A mass of 200 g was allowed to rest on the upper glass slide for 5 min. The raise in the diameter due to gel distribution was noted. The spreadability was then considered from the following formula:

$$\text{Spreadability} = M \times L / T$$

Where, M = mass in grams,

L = distance travelled by gel,

T = time taken in seconds.

Swelling Index: An exact amount of 1 g of gel was placed in contact with the phosphate buffer solution (pH-7.4) in sink condition for 2 h. After 24 h the weight of the swollen gel was noted.

The swelling index of hydrogel was calculated by using the formula:

$$\text{Swelling index} = W_2\text{-}W_1 \times 100 / W_1$$

W_1- weight of polymer (before swelling)

W_2- weight of polymer (after swelling)

Determination of Drug Content: About 1g of the gel formulation containing a drug equivalent to 100 mg was extracted with 30 ml of ethanol. The volume was 100 ml with phosphate-buffered saline (PBS pH 7.4). The solution was filtered. Different concentrations of extracted fucoidan (5-25 µg/ml) were prepared. The absorbance of the standard and sample solutions was measured at 202 nm using a UV-Visible spectrophotometer [17]. The drug content of the formulation was determined using the following equation:

$$\%\ \text{Drug content} = \text{Actual concentration of drug in formulation} / \text{Theoretical concentration of drug} \times 100$$

***In-vitro* Drug Release Studies:** *In-vitro* release study of fucoidan nanosponge-loaded gel was carried out by using the dialysis bag method. The dialysis membrane was previously soaked overnight in a diffusion medium (PBS 7.4). About 1 g of gel formulation was spread inside the dialysis membrane, which is in contact with donor and receptor compartment.

The whole assembly was set up on a magnetic stirrer with continuous stirring and temperature maintained at 37º C. About 5 ml of sample was withdrawn from the receptor medium at specific intervals and replaced with an equal volume of PBS. The samples were collected for an interval of 5 h [18].

The absorbance of the sample was measured at 202 nm by a UV-visible spectrophotometer.

RESULTS AND DISCUSSION: Fucoidan was extracted from *Dictyota bartayresiana* , and the yield was 6.5% w/w. The isolated fucoidan yield was ascertained, which was comparatively low with other species of brown seaweed. This investigation found that fucoidan has a relatively high level of effectiveness. The figure of brown seaweed - *Dictyota bartayresiana* and extracted fucoidan was represented in **Fig. 1** and **Fig. 2,** respectively.

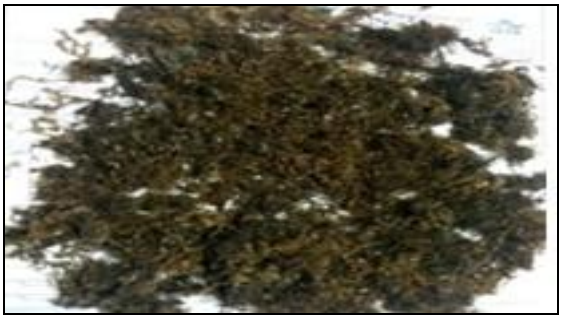


FIG. 1: *DICTYOTA BARTAYRESIANA*

FIG. 2: EXTRACTED FUCOIDAN

Phytochemical Analysis: The phytochemical laboratory analysis of extracted fucoidan revealed the presence of carbohydrates, flavonoids and steroids. Positive results were shown for the sulphate test. The results of the phytochemical analysis are presented in **Table 3.**

TABLE 3: PHYTOCHEMICAL ANALYSIS OF ETHANOLIC EXTRACT OF FUCOIDAN

S. no.	Phytochemical constituents	Ethanolic extract of fucoidan		
		I	II	III
1	Alkaloids	-	-	-
2	Flavonoids	+	+	+
3	Proteins	-	-	-
4	Carbohydrate	+	+	+
5	Saponins	-	-	-
6	Steroids	+	+	+
7	Tannins	-	-	-
8	Sulphate	+	+	+

Spectroscopic Analyses:

Calibration Curve: A calibration curve for concentration versus absorbance (g/ml) was designed. Increasing order of 5, 10, 15, 20, and 25 (g/ml) and its corresponding absorbance were used to achieve linearity. The linearity series was established to be y = 0.037x - 0.003 and regression R^2 = 0.996. The calibration curve is presented in **Fig. 3.**

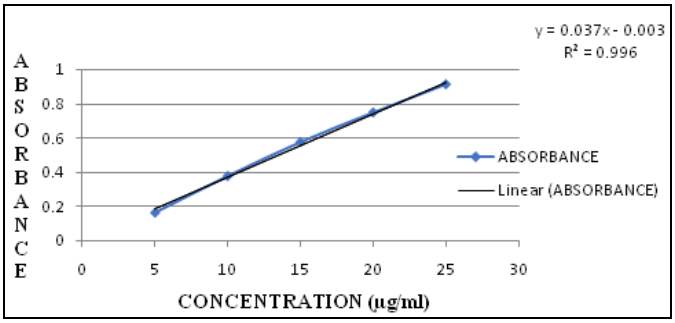


FIG. 3: CALIBRATION CURVE FOR FUCOIDAN

FT-IR Study: The FT-IR Spectra resolves the structural and functional quality of the fucoidan compound. The peak available functional groups have been identified with a corresponding wave number, and the results were interpreted with standard fucoidan spectra. The peak obtained represents fucoidan functional groups at wave number (cm^{-1}). The functional group region of fucoidan is presented in **Table 4,** and IR spectrum is presented in **Fig. 4.**

TABLE 4: FUNCTIONAL GROUP REGION OF FUCOIDAN COMPOUND

S. no.	Wave number (cm^{-1})	Functional groups
1	3683.37	OH group
2	3347.82	C-H stretching
3	1650.77	C=O
4	601.68	C-S stretching
5	2950	Pyran ring
6	1410	S=O stretching

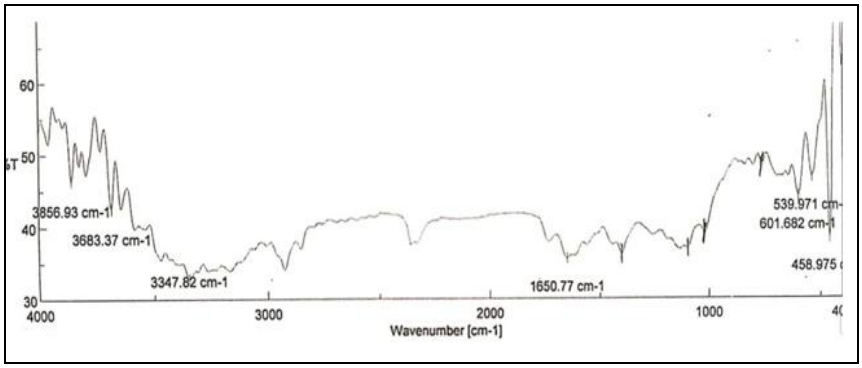


FIG. 4: FT-IR SPECTRUM OF FUCOIDAN

***In-vitro* Study of anti-Arthritic Activity:** The results provide evidence that fucoidan and diclofenac sodium concentrations depend on protein denaturation. The maximum percentage inhibition was observed in the concentration of 1000µg/ml. The inhibitory results of ethanolic extract of fucoidan and diclofenac sodium on protein denaturation are presented in **Table 5** and displayed in a bar graph as shown in **Fig. 5.**

TABLE 5: *IN-VITRO* ANTI-ARTHRITIC STUDY USING PROTEIN DENATURATION ASSAY

S. no.	Concentration (µg/ml)	Percentage inhibition of protein denaturation (% W/W)	
		Diclofenac sodium	Ethanolic extract of fucoidan
1	100	77.77 %	51.86 %
2	200	81.48 %	55.56 %
3	400	88.88 %	59.26 %
4	800	92.59 %	65.19 %
5	1000	96.29 %	85.49 %

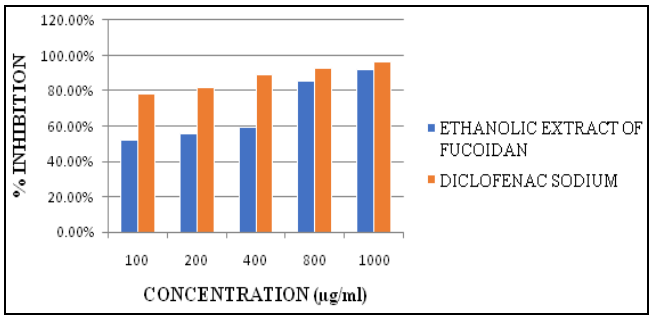


FIG. 5: PERCENTAGE INHIBITION OF PROTEIN DENATURATION ASSAY

FIG. 6: APPEARANCE OF FUCOIDAN NANOSPONGE

Fucoidan Nanosponge:

Appearance: Fucoidan nanosponge obtained was white in colour, spongy in texture, and uniform in size, which are represented in **Fig. 6.**

Physical Compatibility Study: A physical compatibility analysis using FT-IR spectroscopic methods determined that the excipients and drug did not interact in any way. The FT-IR spectrum of fucoidan and polymer is given **in Fig. 7.**

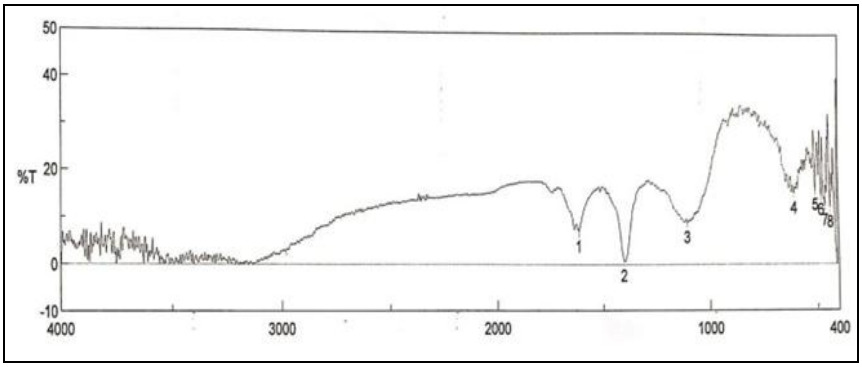


FIG. 7: FT-IR SPECTRUM OF FUCOIDAN AND POLYMER

Fucoidan nanosponge yields depend on the ratio of the drug to the polymer. The yield of the preparation can be varied by adjusting the drug-polymer ratio, cross-linking agent, speed, and temperature. We are examining how the drug-polymer ratio affects nanosponge yield in our current research work.

FT-IR Spectroscopic Analysis of Fucoidan Nanosponge: A peak value in the IR spectrum was used to identify the functional group of the fucoidan and polymer. Based on the standard spectra, the following spectrum can be interpreted. The FT-IR spectrum of fucoidan nanosponge is given in **Fig. 8.**

FT-IR analysis of fucoidan nanosponge indicated that this excipient is compatible with fucoidan and no interactions were observed during the formulation of fucoidan nanosponge.

The FT-IR interpretation of fucoidan nanosponge is presented in **Table 6.**

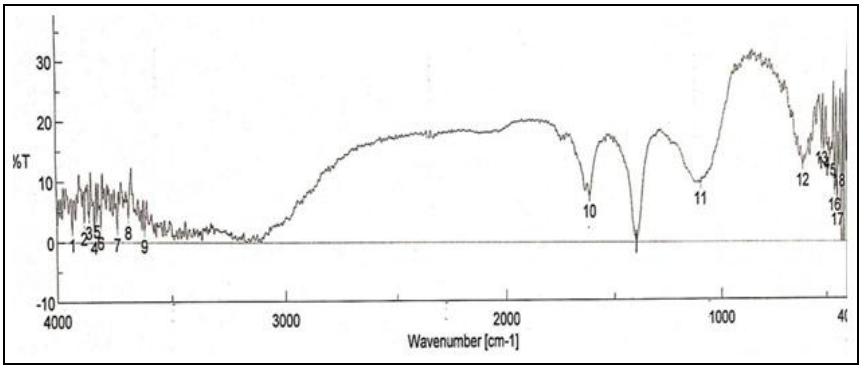


FIG. 8: FT-IR SPECTRUM OF FUCOIDAN NANOSPONGE

TABLE 6: FT-IR INTERPRETATION OF FUCOIDAN NANOSPONGE

Peak Position	Functional Group
3688.19	OH group
3618.77	C-H stretching
1617.02	C=O stretching
1402.11	S=O stretching
614.217	C-S Stretching

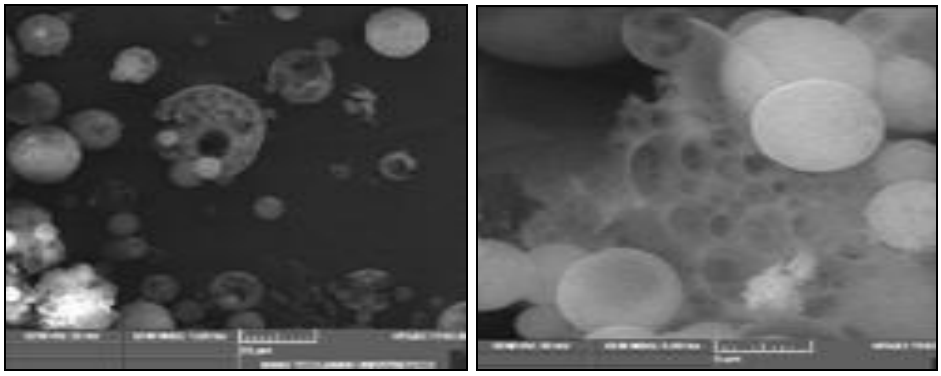
Drug Entrapment Efficiency: Formulation characteristics are considered when determining entrapment efficiency based on the ability of the drug content to be entrapped into a polymer.

Consequently, there was a higher efficiency in percentage entrapment in F1 Formulations. Based on the product yield and drug entrapment efficiency, the F1 formulation was considered the best. The percentage yield and drug entrapment efficiency of all formulations (F1, F2, F3, F4) are presented in **Table 7.**

TABLE 7: PERCENTAGE YIELD AND DRUG ENTRAPMENT EFFICIENCY

Formulation code	Percentage yield (%W/W)	Drug entrapment efficiency (%W/W)
F1	81.66%	79%
F2	63.14%	65%
F3	72.5%	71%
F4	65.55%	60%

Particle Size Measurement: Under scanning electron microscopy, the morphology of nanosponge formulation F1 with the smallest particle size and maximal entrapment efficiency was observed.



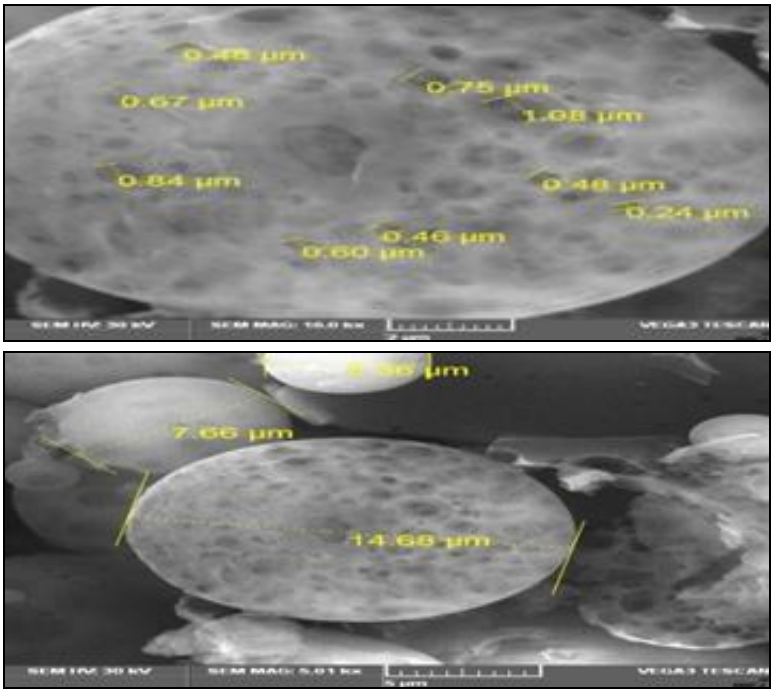


FIG. 9: SEM IMAGE OF FUCOIDAN NANOSPONGE (F1)

The scanning electron microscope (SEM) analysis revealed nanosized, spherical particles with numerous pores on their surfaces.

Fucoidan nanosponge size ranges between 1 µm-20 µm and the porous nature of nanosponge confirmed with a size range of 0.2 µm-1 µm, which are represented in **Fig. 9**, assists the drug release pattern and exhibits effective therapeutic action as fucoidan nanosponge.

Fucoidan Nanosponge Loaded Gel:

Physical Appearance: A gel-like appearance and consistency were observed in the prepared gels, which were transparent, smooth, homogenous, uniform, and homogenous in colour and are represented in **Fig. 10.**

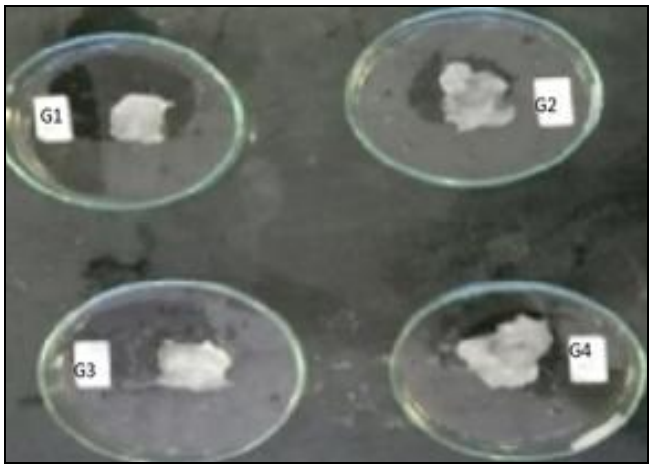


FIG. 10: FUCOIDAN NANOSPONGE LOADED GEL

pH: Gels (G1, G2, G3, and G4) have optimum pH levels based on their skin pH. The gel consistency is appropriate for topical application because it is pH-based.

Viscosity: The viscosity range obtained from all formulations (G1, G2, G3, G4) was considered optimal.

Spreadability: The spreadability of formulations (G1, G2, G3, and G4) was determined to be optimal, with a range of 16-20 (gm-cm/sec). Because of the prepared nanosponge-loaded gel's good spreadability, it is suitable for topical application.

Swelling Index: The swelling index of fucoidan nanosponge-loaded gel indicates the amount of drug released. The swelling studies show that the G4 formulation has a higher swelling index. As a result, the G4 formulation will have an optimal drug release profile for the desired therapeutic effect.

Determination of Drug Content: Drug content refers to the amount of drug present in the nanosponge-loaded gel. G4 formulation has a higher percentage of drug content, based on the results. The higher the drug content, the more drug is released from the formulation. **Table 8** presents the evaluation

TABLE 8: EVALUATION PARAMETERS OF FUCOIDAN NANOSPONGE-LOADED GEL

S. no.	Formulation Code	pH	Viscosity (cp)	Spreadability (g-cm/sec)	Swelling index (%)	Drug content (%)
1	G1	7.0	41.40	16	57 %	65 %
2	G2	7.0	28.20	20	61 %	68 %
3	G3	6.3	31.80	17.45	68 %	66 %
4	G4	6.7	55.20	17.2	73 %	75 %

Parameters of fucoidan nanosponge-loaded gel.

***In-vitro* Drug Release Kinetics Study:** An *in-vitro* release kinetic study was conducted using the dialysis bag method. Increasing drug action with time in a sustained fashion was observed in all formulations. In comparison with other formulations, G4 showed a slightly higher drug release profile at each interval, suggesting a higher drug concentration at the site of action. The G4 formulation shows a Cumulative Drug Release (CDR) percentage of 64.73 % after 5 h. Concentration decreases gradually over an 8 to 12 h period in a controlled manner. *In-vitro* drug release and percentage cumulative drug release of fucoidan nanosponge-loaded gel (G1-G4) are shown in **Table 9** and **Fig. 11.**

TABLE 9: *IN-VITRO* DRUG RELEASE PROFILE OF FUCOIDAN NANOSPONGE-LOADED GEL (G1-G4)

Time (Min)	G1 %CDR	G2 %CDR	G3 %CDR	G4 %CDR
0	0	0	0	0
5	1.8	4.37	2.28	2.9
10	4.2	8.98	4.71	7.19
15	6.96	13.82	7.47	12.16
60	10.6	20.22	10.74	17.35
120	14.8	27.06	14.26	24.31
150	19.08	34.03	18.32	32.05
180	23.69	41.1	22.27	39.9
210	28.44	48.21	27.41	48.11
240	33.55	55.3	32.08	56.42
300	38.86	63.71	37.35	64.73

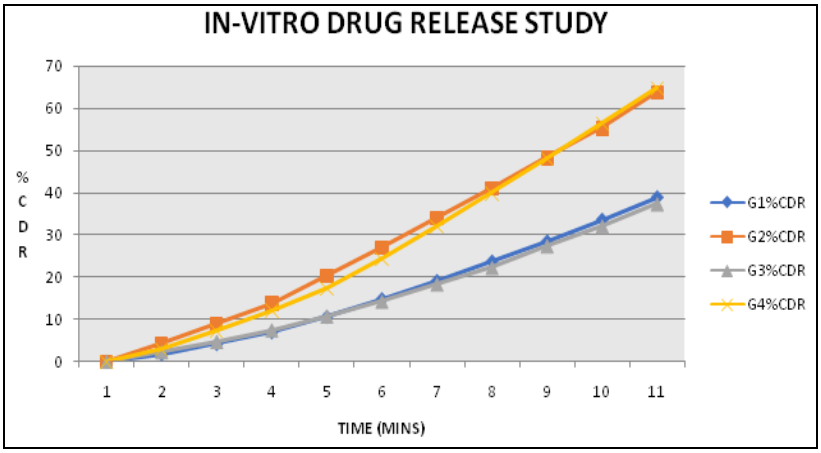


FIG. 11: PERCENTAGE CUMULATIVE DRUG RELEASE OF FUCOIDAN NANOSPONGE LOADED GEL (G1-G4)

Kinetic Data Modelling Analysis: *In-vitro* release kinetics data of optimum formulation G4 were fitted to zero order, first order, Higuchi model, and Korsmeyer-Peppas model using mathematical functions for the determination of possible release kinetics order and mechanism of drug release [19]. The dissolution profile of the formulation is described by kinetic modelling. The maximum regression value was found for zero-order kinetics based on the coefficient of determination (R2). Hence, zero-order kinetics represents the type of drug release phenomena in fucoidan nanosponge-loaded gel formulations.

The results of these mathematical models for fucoidan nanosponge loaded gel using zero-order, first-order kinetics, Korsmeyer-Peppas, and Higuchi models are presented in **Fig. 12.**

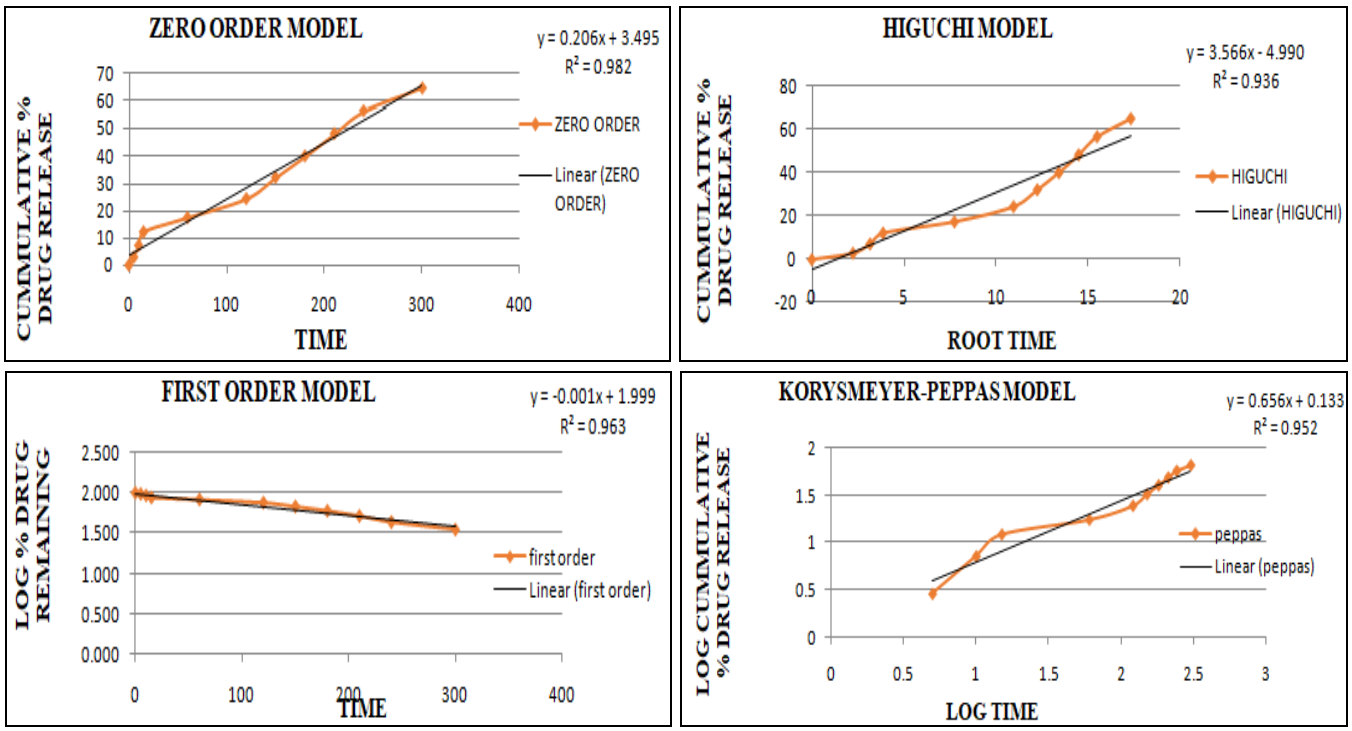


FIG. 12: MATHEMATICAL MODELS OF RELEASE PROFILES OF FUCOIDAN NANOSPONGE LOADED GEL USING ZERO-ORDER, HIGUCHI MODELS, FIRST-ORDER KINETICS AND KORSMEYER-PEPPAS MODELS

CONCLUSION: Fucoidan, a bioactive component of *Dictyota bartayresiana*, was isolated and characterized using spectroscopic methods. In vitro studies of fucoidan indicated 85.49% inhibition of arthritic progression, and it may be an ideal topical drug delivery candidate for arthritis treatment. The formulation F1 demonstrated greater yield and greater entrapment efficiency, which upon morphological analysis shows spherical nanosponge of diameter ranges between 1 µm to 20 µm with numerous pores on the surface of 0.2 µm to 1 µm. We found a zero-order profile with prolonged drug release with the formulation G4 nano sponge-loaded gel fitted to the kinetic model using a mathematical function. Nanogels with targeted characteristics at the desired site of action provide sustained drug release, with the zero-order profile emphasizing controlled drug release. The fucoidan nanosponge-loaded gel is a new methodology for industrial applications because of its nanosized, sustained release profile, better stability, and non-toxic nature. The natural origin of Fucoidan nanosponge-loaded gel and its relatively fewer side effects have a big impact on the market and could lead to a reduction in the use of steroidal drugs.

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