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FORMULATION OF HERBAL TABLET OF *DOLICHANDRONE FALCATA*EXTRACT AND ITS EVALUATION FOR IN-VIVO ANTIULCER ACTIVITY

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ABSTRACT

The purpose of this study was to synthesise and characterise nanoparticles containing extract from the medicinal herb Dolichandrone falcata, which has been shown to have antiulcer capabilities. Dolichandrone falcata was used in the study to extract bioactive chemicals, which were then processed through an optimised process to create nanoparticles. The size, shape, and stability of the nanoparticles were examined using a variety of characterisation methods, such as Zeta sizer, scanning electron microscopy, and transmission electron microscopy. The produced nanoparticles (NF1) showed a particle size range of 1 to 130 nm, with a mean size of 94.3 nm, according to the data. Zeta potential studies showed that the nanoparticles were stable, with a value of -26.8 mV. Images from scanning electron microscopy showed spherical nanoparticles with a consistent size distribution. The Dolichandrone falcata extract was successfully encapsulated by the nanoparticles, as evidenced by their 82.56% entrapment efficiency. Using a lyophilization procedure, the synthesised nanoparticles were then used to create nanoparticulate tablets (F1-F5). Angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio, weight fluctuation, thickness, hardness, friability, and dissolving profiles were among the pre- and post-compression characteristics of these tablets that were methodically assessed. The tablets demonstrated excellent flow characteristics, suitable hardness, low friability, and reliable drug release patterns in acidic environments, indicating that they may be used orally. A pyloric ligation-induced ulcer model was also used to evaluate the antiulcer activity of the nanoparticles loaded with Dolichandrone falcata extract. In comparison to the control group, the animals treated with the extract-loaded nanoparticles showed a significant decrease in ulcer index, a significant reduction in stomach volume and acidity, and an elevation in gastric pH. Standard medication ranitidine showed comparable efficacy in preventing the development of ulcers. With an astounding 81.22% inhibition rate, the extract-loaded nanoparticles demonstrated their exceptional antiulcer efficacy. The safety of the Dolichandrone falcata extract was further supported by acute toxicity testing, which made it possible to determine the right dosages for further research.

KEYWORDS

Dolichandrone falcata, nanoparticles, antiulcer activity, nanoparticulate tablets, in vivo study

INTRODUCTION

In recent years, the Dolichandrone falcata is becoming very vital plant in medical and pharmaceutical industry. Dolichandrone falcata is a small deciduous tree in the family Bignoniaceae. It is endemic to India. Tree attains a height of 15–20 feet. Leaves are compound 2-6 inches long with 3-6 obovate or oval shaped leaflets. Flowers are white and fragrant. The flowering of this occurs in April–May.[1,2] Despite of these applications this plant is yet to be worked out for its chemical composition. The plant has numerous medicinal uses like antiallergic, anti-inflammatory, antioxidant, antiestrogenic, anxiolytic, anticonvulsant, and anti-parasitic. This plant is also used in curing anemia, bloody diarrhea, and also as anthelmintic, analgesic, antiviral, and antifungal agents.[3] The plant is used to prepare snake venom and also used in the treatment of liver disorder. The bark paste of Dolichandrone falcata is applied in case of fractures. The bark juice is used for menorrhagia and leucorrhoea. The leaves of this plant are used as antioxidant, antiestrogenic and anti-diabetic.[4,5]

Natural biopolymers are attractive products of living organisms as they serve a number of different applications for human health due to their biodegradability, such as vaccine delivery, drug development, and food preservatives1.[6,7] Chitosan (CS) is a natural biopolymer and a derivative of chitin. It is obtained from different sources of chitin and differs on the basis of its degree of deacetylation . In the last few years, CS nanoparticles (CSNPs) have drawn much attention due to their biodegradability, biocompatibility, quantum size effects, large surface to volume ratios, and their simple and inexpensive production. Different biological activities of CSNPs have been reported, such as antimicrobial, antioxidant, anticancer, drug delivery, tissue engineering, carbon nanotube, food preservative, and purification of water.[8,9] Herbal Nanoformulation enhances the target selective activity of the loading drug in vivo, hence making it a promising delivery system for herbal medicine. Today tablets are the most common pharmaceutical dosage forms. Those are popular for the following reasons such as convenient to handle because they are portable and easy to be administered, the cost of manufacturing, packaging and shipping is relatively low from the manufacturers point of view.[10,11]

MATERIALS AND METHODS

2.1. Chemical Reagents

Petroleum ether, Ethanol, Methanol, Dichloromethane, n-hexane, Ethyl acetate, Glacial acetic acid, N-Butanol, Chloroform, Acetone, Formic acid, Benzene, Dimethylsulphoxide (DMSO), conc. Sulphuric acid, Hydrochloric acid, Benzene, pyridine, toluene, anisaldehyde, calcium chloride, copper sulphate, Ferric chloride, Follin's reagent, Iodine, Lead acetate, Magnesium chloride, Mercuric chloride, Ninhydrin, Nitric acid, Phloroglucinol, Potassium iodide, Potassium Dichromate, Potassium sodium Tartarate, Ruthenium red, Sodium acetate, Sodium iodide, Sodium hydroxide, Sodium nitroprusside, Hide powder, Folin Ciocalteu reagent, Sodium bicarbonate, Gallic acid and all the chemicals and reagents are analytical grade (Research lab

Fine Chemicals Pvt. Ltd Mumbai, SD Fine Chem Mumbai, and Merck, India) were purchased from local suppliers.

2.2.Plant Preparation, Extraction, and Phytochemical Analysis

Method: Continuous hot Soxhlet extraction.

The plant material was collected and dried in the shade. Then the dried material is pulverized in grinder. The powdered material was passed through 120 mesh sieves to remove fine powder and course powder was used for extraction. The extraction was carried out with selected solvent Methanol, ethanol and chloroform. The extraction was carried out in Soxhlet extractor till all the constituents were extracted. The completion of extraction was indicated by taking sample of siphon tube on TLC plate and placing it in iodine chamber. Absence of colored spot on plate indicated complete extraction. After completion of extraction, solvent was distilled off and concentrated extract was air-dried. The extract was stored in airtight container. The same procedure was followed during extraction with other solvents. After Methanol, Ethanol (95%) extraction the exhausted marc was kept in oven to remove the solvent completely. Finally, the same dried powdered material was extracted with chloroform.

2.3.Green synthesis of dolichandrone falcata extract loaded chitosan nanoparticle

The chitosan nanoparticle was prepared according to the ionic gelation method using sodium tripolyphosphate (TPP) as cross linker with slight modification. After complete dissolution of 250 mg of chitosan in 1.6% acetic acid, *dolichandrone falcata* extract (5%) was added to this solution (Whole 100ml was added) with magnetic stirring for half hour at 800 RPM. Then TPP (0.5%) was added in drop wise through syringe at a uniform rate. It was further stirred for 2 hours followed by centrifugation for 10 min at 10000 rpm. Supernatant was discarded and residue was re-suspended in phosphate buffer saline (PBS). The nanoparticle was collected. The prepared nanoparticle was lyophilized and stored at 4^0C until further use.

2.4.Characterization of nanoparticles

Zeta potential study

A zeta sizer was used to examine the zeta potential (surface charge) of chitosan nanoparticles. The produced chitosan nanoparticle formulations (NF1-NF2) were diluted with water (0.1ml) and put in an electrophoretic cell with a 15.5 V/cm electrical field to evaluate their zeta potential. Each sample was measured in three different ways.

Scanning electron microscopy

Scanning electron microscopy was used to examine the nanoparticle's morphology. In a first stage, 100l of chitosan nanoparticle formulations were applied to a 10mm glass slide and dried overnight at room temperature in a vacuum desiccator till SEM examination was done. Nanoparticles were mounted on appropriate support and coated with gold using a gold sputter module in a higher vacuum evaporator for analysis. At a voltage of 15kv, observations were made at various magnifications.

Drug entrapment efficiency

The ultra-centrifugation technique was used to assess the drug entrapment effectiveness of chitosan formulations. Using ultracentrifugation at 10,000 rpm for 30 minutes, chitosan

nanoparticle was separated. The pellets were re-dissolved in distilled water, and the supernatant was scanned with a UV-visible spectrophotometer in this parameter.The drug encapsulation efficiency was determined by using the relation in this equation.

% Drug entrapment efficiency= experimental drug contentx100/Theoretical drug content

Production yield of nanoparticles

The yields of nanoparticles were determined by comparing the whole of nanoparticle formed against the combined weight of the copolymer and drug.

% Yield calculation = Amount of drug X100 / Amount of drug +polymer

Transmission electron microscopy

Transmission electron microscopy (TEM) was used to characterize the morphology of AgNPs (JEOL-JEM 2100, 1.4 Angstrom Unit, Tokyo, Japan). Drops of diluted AgNP solutions were air-dried on carbon sheets supported by copper grids to create the samples. Under the microscope, TEM images were seen at 120 kV.

Stability of Nanoparticle

The stability of the produced nanoparticles was evaluated by keeping the optimum formulation in a stability chamber (at 4°C) for three months. The particle size, zeta potential, entrapment efficiency and physical appearance were determined at different time intervals of one, two and three months. (According to ICH Q1A).

2.5.Formulation of tablets

Extract powders of nanoparticles from *Dolichandrone falcata* (NF1) were used in the current investigation. Individual powdered extracts of *Dolichandrone falcata was* used to make five formulations. Then, using a mixture of the various extracts, a formulation was created. The following is the structure of a formula.

Table 6. Formulation containing Nanoparticles of extracts of *Dolichandrone falcata*.

Sr. No.	**Ingredient**	**F1**	**F2**	**F3**	**F4**	**F5**
1	Powder of *Gymnema Silvestre*	125	100	75	50	25
2	Lactose	65	90	115	140	165
3	Talc	5	5	5	5	5
4	Starch	35	30	35	30	35
5	Microcrystalline Cellulose-101	15	20	15	20	15
6	Sodium benzoate	5	5	5	5	5

Quantity of per tablet (mg) Total Weight – 250mg

Preformulation studies

*2.6.*Preformulation Study

1. Angle of Repose-ɵ

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

2. Bulk density (BD)

Bulk density is defined as the mass of a powder to the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape and the tendency of the particles to adhere to one another.

3. Tapped density (TD)

It is the ratio of total mass of powder to the tapped volume of powder

4. Carr's Index:

It is a simple test to evaluate the BD and TD of a powder and the rate at which it was packed down.

5. Hausner's ratio-

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula

*2.7.*Evaluation of the tablets

a. Standardization of size and shape

The diameter and thickness of the manufactured tablet are indicators of the size and shape of the tablets. In the present study, 20 tablets from each manufactured batch were randomly checked for diameter and thickness

b. Weight Variation test

10 tablets were selected randomly and weight individually. The average of tablets is calculated using formula.

c. **Thickness:**

Thickness of the tablets (n=3) was determined using a Vernier Calliper.

d. **Hardness test**

Hardness of the tablet was determined by using the Monsanto hardness tester (n=3) the lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

e. **Friability test:**

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting.

f. Assay of Tablet (Drug content)

Weigh and finely powder not less than 20 tablets. Transfer an accurately weighed quantity of the powder equivalent to about 10mg of powder in 100ml volumetric flask. (33.33mg of powder) Add little amount of methanol, and sonicate the solution for 30 min. Then make up the volume up to mark by using methanol. Filter the solution through the whatmann filter paper to get the clear solution. (100ppm solution of powder - Stock solution) Withdraw 0.8ml, 1.0ml and 1.2ml of the stock solution (100ppm solution of powder) to prepare 8ppm, 10ppm and 12ppm solution respectively. Measure the absorbance spectrphotometrically by scanning wavelength in the range 400nm to 200nm, using methanol as blank. Note down the absorbance.

g. Dissolution studies:

Dissolution study for formulated batches F1-F5 was performed as per USP.

Procedure-

For acid stage

900 of 0.01N Hydrochloric acid with 0.5% Sodium lauryl sulphate was placed in the vessel and the USP-II apparatus (paddle method) was assembled. The medium was allowed to equilibrate to temperature 37±0.5°C. A tablet of each batch was placed in the vessel and was covered; the apparatus was operated up to 02 hrs at 50 rpm. The 2ml of sample was withdrawn at 0, 0.5, 1 and 2hrs.After withdrawing the sample, it was replaced with the fresh 2ml of medium. Absorbance of the sample solution was measured at 206nm by using UV spectroscopy.

*2.8.*In-vivo Study

The in-vivo study was conducted in accordance with the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA, Government of India) guidelines and approved by the Institutional Animal Ethics Committee (IAEC), Gaurishankar Institute of Pharmaceutical Education and Research, Limb, No. GIPER/IAEC/22/08 Dated 20/08/2022.

Animal

Wistar mice weighing 20-30g will be obtained. The animals will be maintained in proper conditions, at temperatures of 25 ± 1°C, a 12-hour light/dark cycle, and a relative humidity of 44-56%, and will be fed with standard rodent diet and water ad libitum. Animals will be fasted for 12-24 h but need to have free access to water up to 1 h before the commencement of the induction of ulcers.

Acute Toxicity Studies

The toxicity tests were performed according to the OECD Guidelines protocol (423). Randomly selected and labelled for individual identification were the 4-6 weeks of old female mice with body weights of between 20-30 g. The room temperature was kept atmospheric [25 ± 2 ° C, RH (50 ± 5 percent)]. Conventional rodent laboratory diet was used for feeding. For common dosing and laboratory environments, animals had been held in the testing room with cages for seven days before. Animals had been fasted 24 hours before dosing.

Test samples were given orally in a single dose using orogastric tube. The sample was given for a group of five female mice, e.g. (5000 mg / kg wt for limit testing) at a predetermined dose. Animals were observed separately during the first 30 minutes after injection, regularly over the first 24 hours, with particular attention during the first 4 hours.

Dose Selection

Dose was determined by the process of up-down control. Limit tests were conducted using *Dolichandrone falcata* extract loaded chitosan nanoparticulate tablets. No mortality was observed at dose 5000mg / kg, hence 10% of the maximum dose was chosen, i.e. 500mg / kg and 100mg / kg was lower in the sample.

Antiulcer activity

Animal

Wistar rats weighing 150-200 g will be obtained. The animals will be maintained in proper conditions, at temperatures of 25 ± 1°C, a 12-hour light/dark cycle, and a relative humidity of 44-56%, and will be fed with standard rodent diet and water ad libitum. Animals will be fasted for 12-24 h but need to have free access to water up to 1 h before the commencement of the induction of ulcers.

Group

The rats will be randomly divided into 5 groups (n = 6) in the study. Each rat in the respective group received distilled water (control), or ranitidine 20 mg/kg b.w intraperitoneally (i.p.) (reference standard), and extract 200-400mg/kg.

Pyloric Ligation-Induced Ulcer Model

The experiment will be conducted according to the method described earlier. After the 7th day of drug administration, the rats will be fasted for 24 h. Phenobarbitone will be used as anesthetic agent and used to make a midline abdominal incision so as to ligate the pylorus without causing it any traction or damage to its blood supply. The stomach will be replaced carefully and the abdominal wall needs to be closed with sutures. The rats will be deprived of water during the postligation period. Four hours after the procedure, the rats will be sacrificed, and the stomachs will be dissected out and cut open along the greater curvature so as to determine the ulcer index (UI) by the Ganguly and Bhatnagar method. The volume of the gastric content will be measured after centrifugation, while the acidity was determined by titration with 0.01 N NaOH using Toppfer's reagent and phenolphthalein as indicators. The percentage inhibition (PI) of the ulcer production will also calculated.

$$\mathrm{PI} = \frac{\text{UI of the control group} - \text{UI of the treatment group}}{\text{UI of the control group}} \times 100.$$

Animals required

a. Species and Strain: Wistar rats

b. Age and Weight: 150-200 g.

c. Gender: Male

d. Number to be used (Year-wise breakups and total figures needed to be given in tabular form)

Sr. No	Name of group	Treatment	No. of animals
1	Normal group	Tween 80	6
2	Standard	Drug	6
3	Formulation (Group 3)	Formulations	18

RESULTS& DISCUSSION

Characterizations of Nanoparticles

The prepared nanoparticles of extract of *Dolichandrone falcata was* subjected for different evaluations parameters.

Particle size determination by Zeta sizer

The particle size of nanoparticles (NF1) made from extracts of *Dolichandrone falcata* were determined. The nanoparticle's particle size was determined to be between a range of 1-130nm.

Table 15: Particle size and zeta potential of extract of *Dolichandrone falcata*

Sr. No.	Sample	Nanoparticle Size (nm)	Zeta Potential (mV)
1	Extract of *Dolichandrone falcata* -NF1	94.3 ± 15	-26.8

Values are shown as the mean ± standard deviation; n=5.

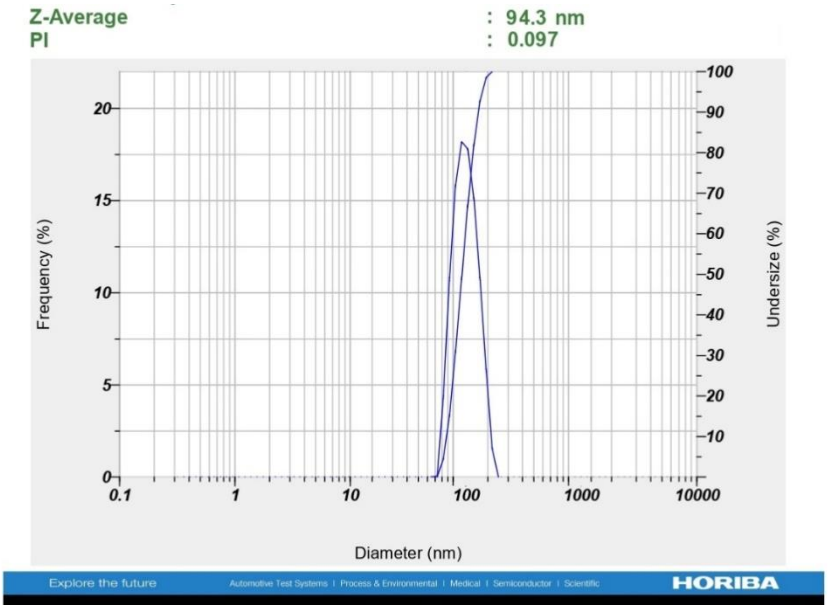
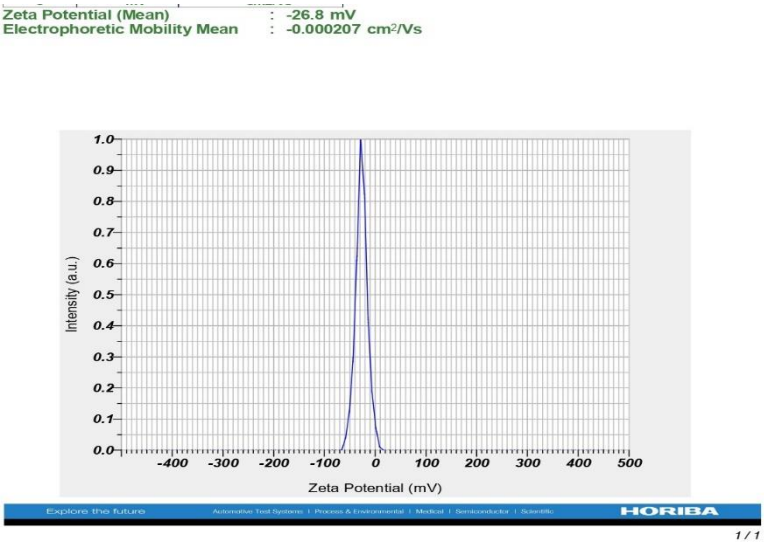


Figure 9. Particle Density Index of extracts derived extract of *Dolichandrone falcata* loaded nanoparticles (NF1).

Particle Density Index of extracts derived extract of *Dolichandrone falcata* loaded nanoparticles NF1 was found to be 94.3nm 1nm respectively. The Particle Density Index of NF1 is found to be within range of nanoparticles size, so the trial 1 of formulation of nanoparticles is considered as optimized procedure. Hence, nanoparticles formulation by Trial 1 procedure is considered for further evaluation.

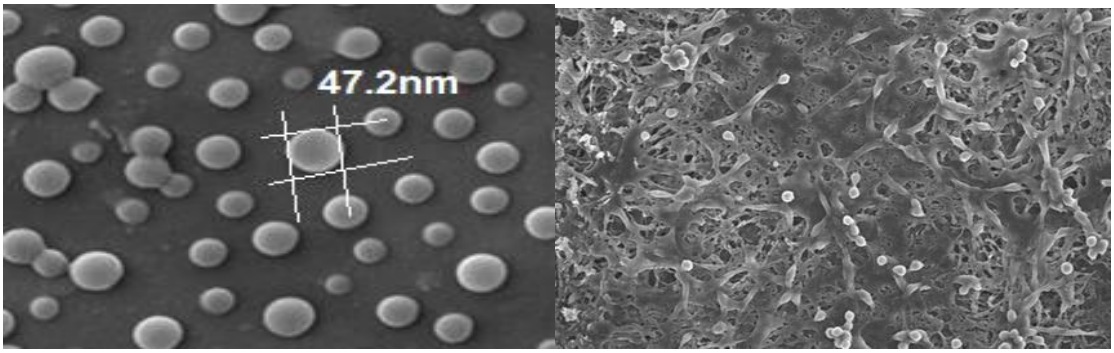
Figure 15. Zeta particle size distribution peak of nanoparticles of extract of *Dolichandrone*



falcata (NF1).

Scanning electron microscopy

Scanning electron microscopy was used to examine the surface morphology of silver nanoparticles. The researchers were able to gain a better grasp of the nanoparticle's morphological features as a result of their research. A high number of nanoparticles with a roughly spherical form were present, and they will split from one another. SEM picture of a freeze-dried silver nanoparticle with a longer cross-linking period, showing a tiny, spherical nanoparticle with a small size.



(a) (b)

Figure 23. Scanning electron micrograph of nanoparticles (NF1) obtained by extract of *Dolichandrone falcata.*

Drug entrapment efficiency

The entrapment efficiency of *Dolichandrone falcata* extract loaded nanoparticle was observed 82.56%, indicating higher drug entrapment efficiency.

Table 16. % Entrapment efficiency of formulation NF1

Formulations	Entrapment efficiency (%)
NF1	82.56

Production yield of nanoparticles

Table 17. Production yield of all formulation (NF1)

Formulation	Production yield (%)
NF1	72.41

Transmission electron microscopy

Below is a TEM micrograph of all nanoparticles (NF1) samples.

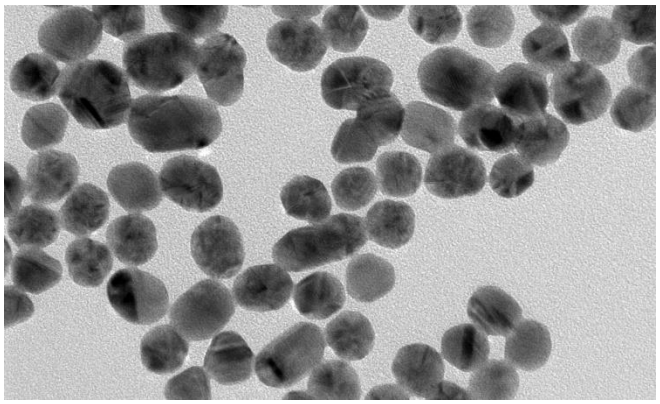


Figure 30- TEM of formulation NF1.

Stability of Nanoparticles-:

After 12 weeks, the stability of the silver nanoparticles of optimized formulations NF1 were evaluated by analysing its absorption spectra. There were no significant changes over the storage period, and the nanoparticles did not agglomerate, indicating that they were more stable.The pattern of change in entrapment efficiency, particle size and zeta potential were same for prepared nanoparticles. There is slight increase in the size of the nanoparticles (1.5%) was observed after three months of storage at 4°C. The entrapment efficiency of nanoparticles was decreased by about 1-4%, whereas zeta potential was found to be decreased by 6%. The changes observed during the storage are negligible.

Table 18. Effect of storage on particle size, zeta potential and entrapment efficiency of Nanoparticles (n=3). Values are expressed as mean ±SD

Storage time		**"0" Month**	**"1" Month**	**"2" Month**	**"3" Month**
Particle size (nm)	NF1	94.3	91.1	87.5	84.6
Zeta potential (mV)	NF1	-26.8	-25.78	-21.27	-20.5

Entrapment efficiency (%)	NF1	82.56	81.22	78.21	75.52

(n=3). Values are expressed as mean ±SD

Evaluation of Nanopaticulate tablet

The prepared lyophilized nanoparticle powder blends of NF1 formulations taken to formulate the tablet (F1-F5) and to carry out the pre formulation study.

9.12.1 Preformulation study-:

- **Organoleptic studies**

Powder of blend was found to be white.

Pre compression parameters-:

1. Angle of Repose-ɵ

Table 19: Pre compression evaluation parameters- Angle of Repose (ɵ)

Batch	**Sample weight (gm)**	**Height of pile (h) in cm**	**Radius (r) in cm**			**Angle of Repose (θ)**			**Mean θ**	**S.D (+-)**	**Angle of repose**
						θ1	**θ2**	**θ3**			
			r1	**r2**	**r3**						
F1	5.001	1.5	2.6	2.7	2.8	29.68	28.81	27.92	28.80	±0.8	Excellent
F2	5.002	1.6	2.8	2.6	2.8	29.68	31.38	29.68	30.24	±0.9	Excellent
F3	5.004	1.5	2.8	2.7	2.8	27.92	28.81	27.92	28.21	±0.5	Excellent
F4	5.004	1.6	2.6	2.8	2.6	31.38	29.68	31.38	30.81	±0.9	Good
F5	5.004	1.6	2.6	2.6	2.7	31.38	31.38	30.54	31.10	±0.4	Good

±S.D. n=3

2. Bulk density

Table 20. Pre compression evaluation parameters- Bulk density

Batch	Mass of powder M (gm)	Bulk volume of powder V_0			Bulk density Db			Mean Db	S.D. ±
		V_{01}	V_{02}	V_{03}	Db1	Db2	Db3		
F1	25.001	60	61	59	0.42	0.41	0.42	0.41	±0.005
F2	25.002	60	61	59	0.42	0.41	0.42	0.41	±0.005
F3	25.004	60	61	59	0.41	0.41	0.42	0.41	±0.005
F4	25.003	60	61	59	0.41	0.41	0.42	0.41	±0.005
F5	25.002	60	61	59	0.42	0.41	0.42	0.41	±0.005

±S.D. n=3

3. Tapped density (TD):

Table 21. Pre compression evaluation parameters- Tapped Density.

Batch	Mass of powder M (gm)	Bulk Volume	Tapped volume of powder V_t			Tapped density Dt			Mean Dt	S.D. ±
			V_{t1}	V_{t2}	V_{t3}	Dt1	Dt2	Dt3		
F1	25.002	60	61	59	0.42	0.41	0.42	0.41	±0.005	25.002
F2	25.001	60	61	59	0.42	0.41	0.42	0.41	±0.005	25.001
F3	25.004	62	61	59	60	0.41	0.42	0.41	0.42	±0.005
F4	25.002	62	61	59	60	0.41	0.42	0.41	0.42	±0.005
F5	25.004	62	61	59	60	0.41	0.42	0.41	0.42	±0.005

±S.D. n=3

4. Carr's Index:

Table 22. Pre compression evaluation parameters- Carr's Index

Batch	Tapped Density (Dt)	Bulk Density (Db)	Carr's Index 100 x (Dt)-(Db)/ (Dt)	Flow Character
F1	0.42	0.41	2.38	Excellent
F2	0.43	0.41	4.76	Excellent
F3	0.42	0.41	2.38	Excellent
F4	0.42	0.41	2.38	Excellent
F5	0.42	0.41	2.38	Excellent

5. Hausner's ratio-

Table 23. Pre compression evaluation parameters- Hausner's ratio

Batch	Tapped Density (Dt)	Bulk Density (Db)	Hausner Ratio	Flow Character
F1	0.42	0.41	1.02	Excellent
F2	0.43	0.41	1.05	Excellent
F3	0.42	0.41	1.02	Excellent
F4	0.42	0.41	1.02	Excellent
F5	0.42	0.41	1.02	Excellent

Evaluation of Tablets (Post compression parameters)

1. Organoleptic properties

All batches **(**F1-F5) were assessed for organoleptic properties like color, odor, and taste and found to be acceptable in all aspect.

General appearance: The formulated tablets were assessed for its general appearance and observations were made for shape, colour and texture.

a. Shape- Round

b. Colour- Whitish

c. Texture- Smooth

From the results obtained it was found that F1-F5 formulations has hardness, weight variation & friability within IP limit.

2. Weight Variation

Table 24. Weight variation test- F1-F5

Sr. No.	Parameter	F1	F2	F3	F4	F5
1	Weight variation (%)	2.52	2.27	2.56	2.71	2.90

3. Thickness

Table 25. Tablet parameters (Batch F1-F5) - Thickness.

Batch	Thickness in mm n=3				S.D.
	1	2	3	Mean	±
F1	4.51	4.50	4.50	4.50	±0.005
F2	4.51	4.50	4.50	4.50	±0.005
F3	4.51	4.49	4.49	4.49	±0.011

F4	4.50	4.49	4.49	4.49	±0.005
F5	4.51	4.50	4.50	4.50	±0.005

±S.D. n=3

4. Hardness test:

Table 26. Tablet parameters (Batch F1-F5) - Hardness test.

Batch	**Hardness in kp n=3**				**S.D. ±**
	1	**2**	**3**	**Mean**	
F1	5.3	5.4	5.4	5.3	±0.057
F2	5.5	5.4	5.4	5.4	±0.057
F3	5.5	5.5	5.4	5.4	±0.057
F4	5.5	5.5	5.4	5.4	±0.057
F5	5.7	5.4	5.4	5.5	±0.173

±S.D. n=3

5. Friability test:

Table 27. Tablet parameters (Batch F1-F5) - Friability test.

Batch	**weight of tablets before test (W1)**	**weight of tablets after test (W2)**	**Friability % %Friability = [(W1-W2)/W1] × 100**
F1	2.505	2.501	0.13
F2	2.509	2.505	0.10
F3	2.508	2.501	0.14

F4	2.507	2.503	0.10
F5	2.507	2.500	0.14

6. Dissolution Study-:

Dissolution data of matrix tablets are reported in below respective tables. Dissolution study for each formulation was carried out in triplicate, in HCl.

Table 29. Dissolution profile (F1-F5)

Time in Min	F1	F2	F3	F4	F5
0	0	0	0	0	0
10	26.24	25.05	26.1	8.45	11.24
15	33.56	32.69	32.99	16.57	25.18
30	67.34	65.57	67.51	40.21	46.55
45	72.00	70.62	71.26	64.54	68.33
60	88.25	86.59	81.47	80.54	78.59

± S.D. n=3

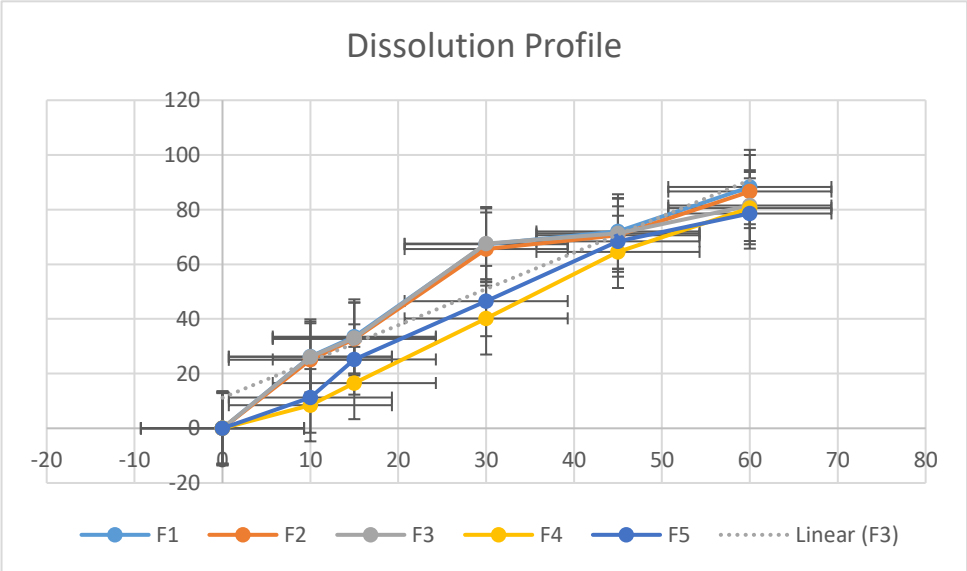


Table 37. Dissolution profile (F1-F5)

Stability Study (Accelerated study)

For all Formulation, an accelerated stability study was conducted in accordance with ICH stability recommendations. Hardness, cumulative percent drug release, wt variation. Friability etc parameters were checked. The look, texture, and colour of prepared tablets from batch F1-F5 upto stability duration did not vary. Other parameters were found satisfactory during stability study.

Table 29. Dissolution Study Data of stability study (F1-F5)

Formulation	Test/Parameter	Accelerated Stability Testing				
		Initial	**First month**	**Two month**	**Third month**	**Sixth month**
F1	**Appearance**	Off white	Off white	Off white	Off white	Off white
	wt. variation (%)	4.75	4.60	4.45	4.39	4.50
	Dissolution (%)	91.5	93.9	92.01	92.18	92.11
F2	**Appearance**	Off white	Off white	Off white	Off white	Off white
	wt. variation (%)	4.72	4.63	4.60	4.52	4.40
	Dissolution (%)	90.4	93.5	91.45	92.05	91.58
F3	**Appearance**	Off white	Off white	Off white	Off white	Off white
	wt. variation (%)	4.35	4.32	4.27	4.20	4.12
	Dissolution (%)	89.56	92.54	90.45	91.56	91.25
F4	**Appearance**	Off white	Off white	Off white	Off white	Off white
	wt. variation (%)	4.25	4.22	4.18	4.15	4.12
	Dissolution (%)	89.11	92.10	90.25	91.02	90.56
F5	**Appearance**	Off white	Off white	Off white	Off white	Off white
	wt. variation (%)	4.68	4.62	4.55	4.48	4.40
	Dissolution (%)	88.69	91.54	89.66	90.26	89.75

Acute Toxicity Study

Table: Acute toxicity study data of extracts of *Dolichandrone falcata* plant for each animal.

Sr. No.	Body wt. (gm)	Dose mg/kg	Sign of toxicity					Mortality
			Ataxia	Convulsion	Motor activity	Dyspnoea	Rigidity of tail	
1	22.8	5000	--	--	--	--	--	NO
2	24.5	5000	--	--	--	--	--	NO
3	22.5	5000	--	--	--	--	--	NO
4	23.2	5000	--	--	--	--	--	NO
5	24.5	5000	--	--	--	--	--	NO

From above results it can be concluded that the ethanolic extracts of *Dolichandrone falcata* is safe up to the dose of 5000 mg/kg. 1/10th of this LD50 was taken as an effective dosefor subsequent studies.At dose 5000mg/kg no mortality was observed and hence 10% of the limit dose i.e. 500mg/kg and a lower dose of 250 mg/kg were selected for studies. The dose 200mg/kg and 400mg/kg was used for the further studies.

Antiulcer activity

Pyloric Ligation-Induced Ulcer Model

Aqueous suspension of ethanolic extracts of *Dolichandrone falcata* (250mg/kg) was tested. The results obtained from the effect of combined ethanolic herbal extracts in pylorus ligation were shown in Table below and Figure.

In control animals, without any drug pH was 1.58±0.67. Ethanolic extract shown significant rise in pH 4.15±0.25 as compared to control. Ranitidine (20mg/kg), standard drug was shown pH to 5.2 ±1.25. This was more potent than the extracts used. The gastric volume has been decreased 2.98±0.88 and 2.78± 0.26 in ethanolic extract and ranitidine compared to control (6.15 ± 0.35). Gastric free acidity was found 21.56±1.25, 6.5±0.98 and 4.25±1.65 mEq/liter in control, standard and extract treated animals respectively. Ethanolic extract shown significantly reduced free acidity as compared to control, whereas similar potency with ranitidine in decreasing gastric acidity. Ranitidine (27.85±2.54 mEq/L) and ethanolic extract (31.35±1.85 mEq/L) shown significant reduction in total acidity compared to control (59.15±2.51 mEq/L). In measurement of ulcer index, ethanolic extract (2.1±0.58) shown significant lower ulcer index compare to control (13.32±1.25) and ranitidine (2.8±0.51). Percentage Inhibition of ulcer formation by

ethanolic extract (81.22±1.25%) was more significant compared to control (0.0%) and ranitidine (80.14 ± 2.45%).

Table: Effect of combined herbal extracts on ulcer induced by pyloric ligation

Treatment	Dose (mg/kg) p.o	Volume of gastric juice (ml/4h)	pH	Free Acidity (mEq/L)	Total Acidity (mEq/L)	Ulcer Index	%Inhibition of ulcer
Control	4 ml/kg	6.15 ± 0.35	1.58±0.67	21.56±1.25	59.15±2.51	13.32±1.25	**0.0**±0.0
Ranitidine STD	20 mg/kg	2.78± 0.26***	5.2 ±1.25***	6.5±0.98***	27.85±2.54***	2.8±0.51***	80.14 ± 2.45***
EDF = Ethanolic extract of *Dolichandrone falcata*	250mg/kg	2.98±0.88**	4.15±0.25**	4.25±1.65**	31.35±1.85**	2.1±0.58***	81.22±1.25***
EDF = Ethanolic extract of *Dolichandrone falcata*	500mg/kg	2.82±0.58***	4.28±0.89**	4.78±1.58**	29.22±1.24***	2.2±0.23***	82.35±0.26***

Where, EDF = Ethanolic extract of *Dolichandrone falcata*; Values are mean ±SD, n = 6 in each group

*p<0.05; **p<0.01; ***p<0.001 when compared with control group.

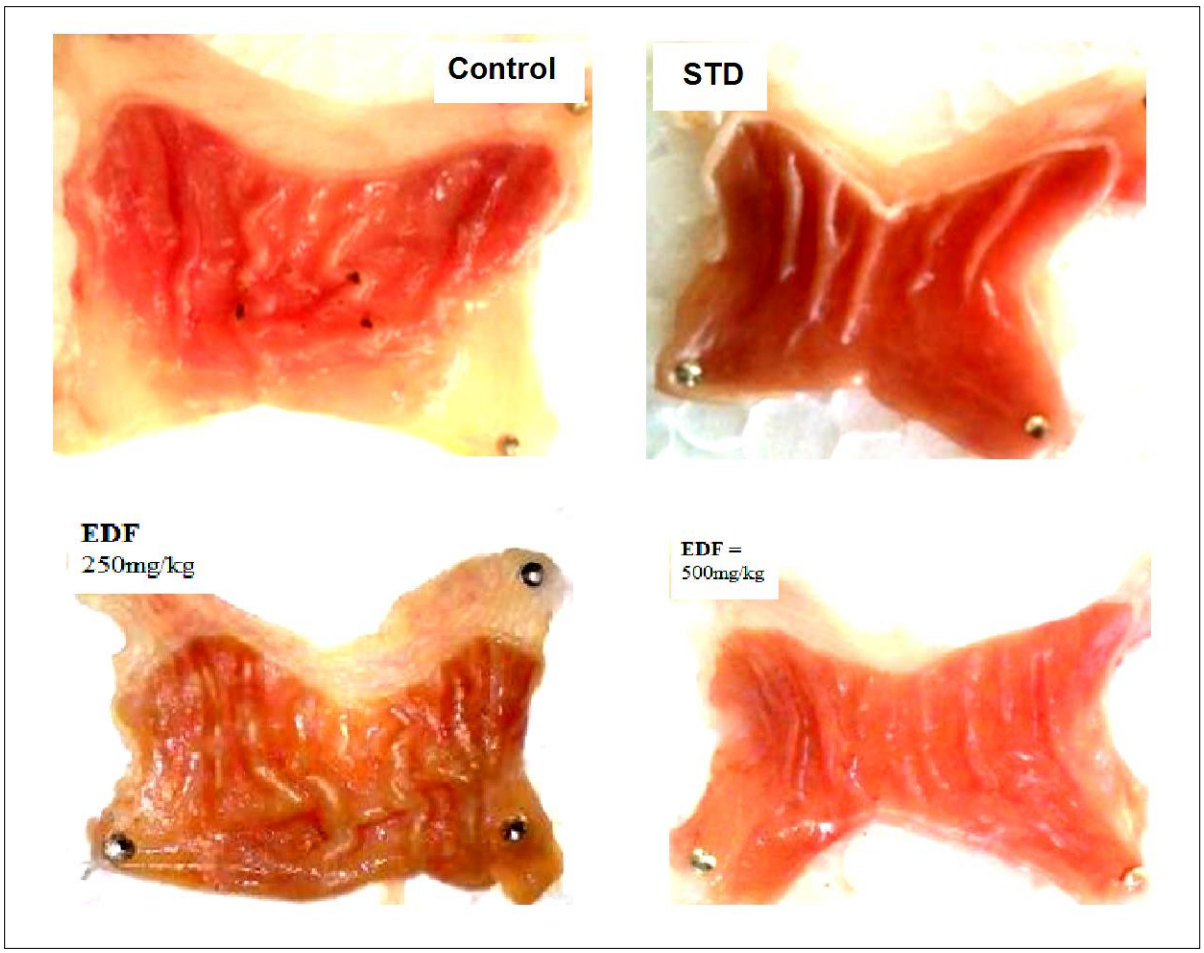


Figure: Effect of herbal extracts in Pylorus ligation induced ulcer

CONCLUSION

This research endeavors into the extraction and formulation of tablets utilizing Dolichandrone falcata, focusing on its antiulcer potential. The study commenced with the characterization of nanoparticles derived from the plant extract, revealing a well-defined particle size range (1-130 nm) and excellent stability over a 12-week period. The SEM analysis underscored the spherical morphology of the nanoparticles, while high drug entrapment efficiency (82.56%) was achieved. Pre-compression studies, including parameters like angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio, indicated excellent flow properties of the formulations (F1-F5). The formulated tablets, F1-F5, exhibited desirable organoleptic properties, hardness, thickness, and friability within acceptable limits. Dissolution studies demonstrated the sustained release of the active ingredient, further confirmed during stability assessments. Notably, even after six months of stability testing, the tablets maintained their physical and chemical integrity. The acute toxicity study established the safety of the ethanolic extracts up to a dose of 5000 mg/kg, paving the way for subsequent experiments.

In the antiulcer evaluation using the pyloric ligation-induced ulcer model, the ethanolic extract of Dolichandrone falcata demonstrated promising antiulcer activity. The extract significantly

increased gastric pH, reduced gastric volume, free acidity, total acidity, and ulcer index. Comparatively, it exhibited a higher percentage inhibition of ulcer formation than the standard drug ranitidine, validating its efficacy.

To conclude, this study showcases the successful development of a stable and effective antiulcer formulation utilizing Dolichandrone falcata. The comprehensive characterization of nanoparticles, coupled with rigorous pre- and post-compression evaluations, strengthens the credibility of the formulated tablets. The demonstrated antiulcer potential emphasizes the plant's therapeutic significance, suggesting its potential application in the pharmaceutical industry. This research contributes valuable insights into the development of natural and safe antiulcer therapies, bridging the gap between traditional knowledge and modern pharmacology.

CONFLICT OF INTEREST

None declared by authors.

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