https://doi.org/ 10.33472/AFJBS.6.9.2024.3627-3644

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Curcumin Phytosomes: Formulation, Evaluation and Physicochemical Characterization

Anuj Agarwal[1]*, Prof. Seema Tomar[2]

anuj2304@gmail.com

1* Research Scholar, Faculty of Pharmaceutical Sciences, Motherhood University, Roorkee.

2 Professor, Faculty of Pharmaceutical Sciences, Motherhood University, Roorkee.

Article History

Volume 6,Issue 9, 2024

Received: 28 Apr 2024

Accepted : 10 May 2024

doi: 10.33472/AFJBS.6.9.2024.3627-3644

ABSTRACT:

Curcumin is a naturally occurring hydrophobic molecule and considered to be therapeutically safe.it is a naturally present polyphenolic compound, belonging to class of flavonoids glycosides. It is also known as diferuloylmethane and has been widely studied for its therapeutic efficacy for many disorders including several inflammatory diseases. However its application is highly restricted due to its poor aqueous solubility, physicochemical instability and inadequate bioavailability.It has anti-inflammatory, antioxidant, anticarcinogenic and antiinfectious properties. The objective of the present study is to formulate curcumin-phospholipid complex and characterize by physicochemical method. Curcumin-loaded phytosomes were prepared by thin film hydration method using rotary evaporator by using soya-lecithin as a phospholipid. The formulation was prepared with a variable drug: soya-lecithin ratios (0.5–2.5), with varying temperature (45–65^{0}C). Design expert software was used for the optimization of Curcumin-loaded phytosomal formulations. Central composite design-based factorial design was applied and evaluated for percentage yield and entrapment efficiency as dependent variables. The effects of drug- phospholipid complex and temperature on percentage yield and entrapment efficiency were studied graphically. The formulations were further characterized with vesicle size, zeta potential and in-vitro release. In-vitro drug release study showed that a maximum of about 90.83% drug was released from the Curcumin-phytosomal formulation at the end of 12 hr. FT-IR analysis, DSC techniques were used to evaluate the drug and soya-lecithin compatibility studies. Scanning electron microscopy showed the uniform structure and spherical shape of the vesicles. Theresults of the study revealed that the Curcumin-soya-lecithin phytosomecomplex may be considered as apromising drug delivery system that improves the absorption and bioavailability of plantconstituents.

Key words: Phytosome, Curcumin, Soya-lecithin, Phospholipid

INTRODUCTION:

Herbal medicines have been widely used all over the world since ancient times and have been recognized by physicians and patients for their better therapeutic value as they have fewer adverse effects as compared with modern medicines. Phytotherapeutics need a scientific approach to deliver the components in a sustained manner to increase patient compliance and avoid repeated administration. This can be achieved by designing novel drug delivery systems (NDDS) for herbal constituents. NDDS not only reduce the repeated administration to overcome non-compliance, but also help to increase the therapeutic value by reducing toxicity and increasing the bioavailability.One such novel approach is nanotechnology. Nano-sized drug delivery systems of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with plant medicines.

However, most of the herbal origin drugs possess insoluble character leading to lower bioavailability and increased systemic clearance requiring repeated administration or higher dose, which makes the drug as a poor candidate for therapeutic use. In phyto-formulation research, developing nano dosage forms such as Phytosomes has large number of advantages for herbal drugs, including enhancement of solubility and bioavailability, protection from toxicity, enhancement of pharmacological activity, enhancement of stability, sustained delivery, protection from physical and chemical degradation, etc.

The use of phytosomes is a new advanced modern NDDS formulation technology to deliver herbal products and drugs by improved better absorption and as a result produce better results than those obtained by conventional herbal extracts. This phytosome technology is a breakthrough model for marked enhancement of bioavailability, significantly greater clinical benefit, assured delivery to the tissues, and without compromising nutrient safety.

A number of hydrophilic and hydrophobic phytonutrients (mainly flavonoids and other polyphenols) can be converted into lipid-friendly complexes by reacting herbal drugs with phospholipids in the form of phytosomes. They are more bioavailable as compared with simple herbal extracts owing to their enhanced capacity to cross the lipid-rich biomembranes and finally reach the blood. Curcumin (CRM) is a naturally occurring polyphenolic compound, belonging to class off lavonoids glycosides. It is a polyphenol known as diferuloylmethane,has been widely studied for its therapeutic efficacy for manydisorders including several inflammatory diseases. It has low bio-availability due to poor absorption and rapid metabolism and elimination.

The aim of the present study is to formulate curcumin-phospholipid complex to enhance its bio-availability and characterize for its physicochemical properties.

MATERIALS AND METHODS:

Materials:

Curcumin and Soya-lecithin were obtained from K Patel Phytoextraction Pvt. Ltd., Mumbai and Konark Herbals & Health Care, Daman respectively. All chemicals and reagents used were of analytical grade.

Methods:

Preparation of Curcumin Phospholipid Complex (Cur-PC):

The Curcumin phytosomes were prepared by refluxing Curcumin and Soya lecithin in different ratios of (1:0.5, 1:1.5, and 1:2.5)**.** Briefly, accurately weighed amounts of Curcumin and Soya lecithin were placed into a 100 mL round bottom flask and dissolved in 20 mL of ethanol. The reaction temperature of the reflux was controlled at 50 °C using a water bath for 3 h. The resultant clear solution was dried at 45°C under vacuum to remove traces of solvents in order to obtain the Curcumin phytosomes. The prepared thin layer had been kept overnight in room temperature prior to hydration. This dried film was hydrated with 10ml distilled water in a rotary at 45°C. The phytosomes were finally sonicated for 4 minutes in a probe sonicator, with 60% amplitude and 5 seconds on-off interval. All phytosomesbatches were stored in the refrigerator. [3-4]

Design of Experiment

A response surface design [Central Composite Design (CCD)] was used to study the influence of independent variables, viz., drug: phospholipids ratio (X1, w: w), and temperature (X2, °C) on the % yield and % entrapment efficiency of Curcumin. The two independent variables (X1 and X2) were selected at three levels resulting in nine possible combinations. The dependent variableswere % yield and % entrapment efficiency of Curcumin. The experimental trials were performed using all nine possible combinations of the selected variables.

The mathematical model containing coefficient effects, interactions, and polynomial terms was analyzed to assess the response using the following equation:

$Y = b0 + b1\ X1 + b2\ X2 – b3\ X1\ *X1 – b4\ X2\ *X2 – b5\ X1\ *X2$

Where Y is the dependent variable, b is the coefficient of the independent variable X. The main effects (X1 and X2) represent the possible aggregate effect of both factors as they change independently from their low to high level. The interaction term (X1 X2) shows how the response changes when two factors are simultaneously changed. The polynomial terms describe the non-linearity. The composition of Curcumin Phytosomes has been depicted by Table 1.

Table 1: Composition of Phytosomes formulations containing different ratios of Curcumin and Soya lecithin:

S. No.	Formulation Code	Drug: Phospholipid ratio	Temperature (^{0}C)	Ethanol (ml)
1	F1	0.5	65	20
2	F2	0.5	45	20
3	F3	1.5	65	20
4	F4	2.5	55	20
5	F5	1.5	45	20

6	F6	2.5	45	20
7	F7	1.5	55	20
8	F8	0.5	55	20
9	F9	2.5	65	20

Characterization of Curcumin-Phospholipid Complex-

The prepared Phytosomal formulations of Curcumin were characterize for Percentage yield, Entrapment efficiency, Particle size, Zeta potential, in-vitro drug release etc.

Percentage yield:

Complexes obtained were dried in desiccator and weighed to note the quantity. Yield (%) was calculated by given formula:

Yield (%) = total amount of complex/total amount of raw material*100

Entrapment Efficiency:

Entrapment efficiency (EE) was measured using UV– visible spectrophotometer (UV-1800, Shimadzu). A weighed quantity of phyto-phospholipid complex Cur-PC equivalent to 10 mg of Curcumin was added to 50 ml methanol in a 100 ml beaker.The contents were stirred on a magnetic stirrer for 4 h and then allowed to stand for one hour. Clear liquid was decanted and centrifuged at 5000 rpm for 15 min. After centrifugation the supernatant was filtered through 0.45 µ whatman filter paper and after suitable dilution absorbance was measured in UV at 430 nm; the concentration of drug was measured. All measurements were performed in triplicate.

The EE (%) was calculated using the following formula:

EE (%) = T-S/T × 100

Where, T- Total concentration of Curcumin, S-is the Curcumin contained in the filtrate. In the present investigation, % yield and % Entrapment efficiency was selected as independent factors which have potential effect on formulation of phytosomes. The selected parameters were analyzed by ANOVA[5].

Particle size and zeta potential determinations

Diameterof particle size was determined by Malvern Zetasizer (equipped with Argon laser) based on principle of laser light scattering. The Zetasizer is equipped with an Argon laser for determination of particle size.Zeta potential was determined by diluting Curcumin with 100 times using distilled water and analyzed using Zetasizer. [7]

FTIR Analysis:

FT-IR spectrophotometry was used for structure analysis of sample. A FTIR spectrum of Curcumin, Soya lecithin, Physical Mixture of Curcumin & Soya lecithin (1:1) and Phytosomal formulation was obtained using FTIR spectrophotometer. About 5-10 mg of samples were scanned by FTIR & infrared

spectrum was recorded in the 4000-400 cm^{-1} region to check the compatibility of Curcumin and selected excipients [1].

Differential scanning calorimetry (DSC):

DSC thermograms of curcumin, Soya lecithin, and Physical mixture were obtained using a DSC-60 instrument. Samples were weighed, transferred to hermetically sealed aluminum pans and heated at a rate of 10ºC/min over a range of 30.00°C to 440.00°C. An indium standard was used to calibrate the instrument and enthalpy scale. An inert atmosphere was maintained by purging nitrogen at a rate of 10 mL/min. [2]

In-vitro dissolution study:

The in-vitro dissolution profiles of Curcumin phytosomes in a USP XXIII, six station dissolution test apparatus, type II (VEEGO Model No. 6 DR, India) at 100 rpm and at 37°C. An accurately weighed amount of Cur-PC of Curcumin 50 mg was put in to 900 ml of pH 6.8 phosphate buffer. Samples (5 ml each) of dissolution fluid were withdrawn at different time intervals and replaced with an equal volume of fresh medium to maintain sink conditions. Withdrawn samples were filtered (through a 0.45 µm membrane filter), diluted suitably and then analyzed spectrophotometrically at 430 nm to determine drug release from the drug phospholipid complex. [5]

Optimization study:

The selected independent variable i.e., drug: phospholipid ratio (Factor A) and temperature (Factor B) were analyzed by ANOVA and based on the responses, the software has suggested a check point batch which was considered as an optimized batch for further evaluation.

Checkpoint analysis:

The experimental and expected results were compared and a checkpoint batch was selected which was further analyzed for evaluation parameters.

The optimized batch thus obtained was further evaluated for various evaluation parameters.

Scanning Electron Microscopy:

External surface morphology was examined by Scanning electron microscopy. The detailed particle structural characterizations and morphologies of formulation were studied by scanning electron microscope. Samples were developed by mounting powder onto a brass stub using graphite glue, then coated with gold under vacuum before use. Images were recorded at an acceleration voltage of 10 KV at the required magnification using a scanning electron microscope.[8]

RESULT AND DISCUSSION:

Preparation of Cur-PC Complex:

The phytosomes of Curcumin were prepared by utilizing different ratios of Curcumin and soya lecithin in different ratios. Ethanol was used as solvent for the preparation of phytosomes. The Design of Experiment was used to optimize the independent variables (drug: phospholipid & temperature) to get

the desired optimized Phytosomal formulation of Curcumin by Central Composite Design.The prepared phytosomes of Curcumin were evaluated for Percentage yield, Entrapment efficiency, particle size diameter and zeta potential, in-vitro drug release.

Percentage yield

The percentage yield of prepared phytosomes was determined and results were reported in table 2.

Table 2: Percentage yield of Phytosomesbatches F1-F9

S. No.	Formulation Code	Yield (%)
1.	F1	70.87
2.	F2	63.53
3.	F3	85.38
4.	F4	83.41
5.	F5	65.84
6.	F6	79.95
7.	F7	76.71
8.	F8	73.81
9.	F9	88.65

In the current investigation, the percentage yield (R1) of the phytosomes ranged from 63.53-88.65 nm, which can be considered an acceptable midrange that imparted reasonable homogeneity and a satisfactory size distribution. The contour plot(Figure 1) and 3D graph (Figure 2) indicated a strong influence of the studied factors on Percentage yield.

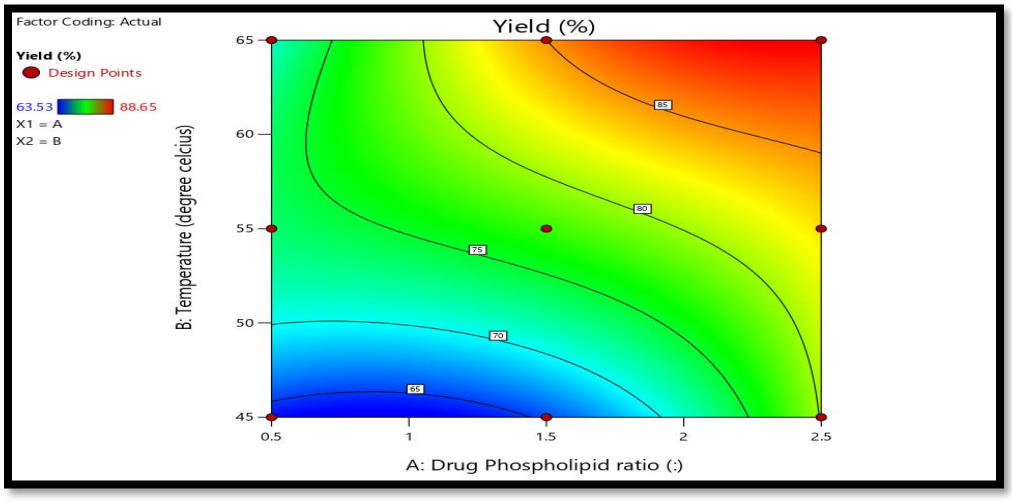

Figure 1: Contour graph showing the effect of Drug phospholipid ratio & Temperature on R1 (Percentage yield)

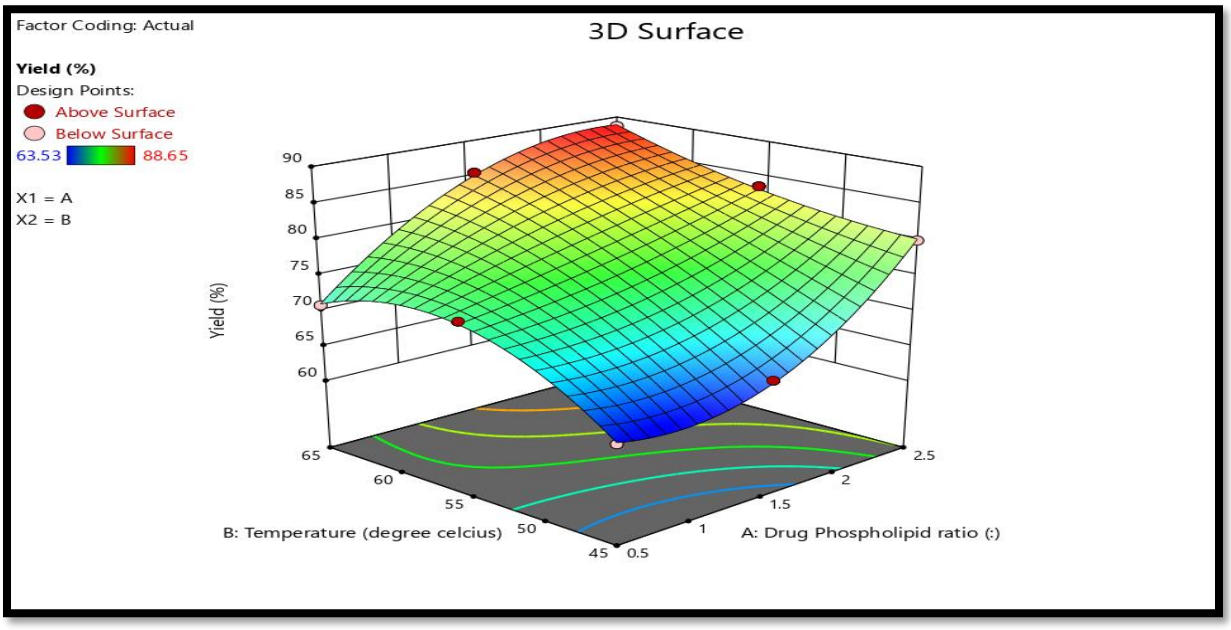

Figure 2: 3D graph showing the effect of Drug phospholipid ratio & Temperature on R1 (Percentage yield)

Entrapment Efficiency (EE)-

Entrapment efficiency of prepared phytosomes was determined and it was found that it was highest with F9 batch which the batch F2 showed least EE.

Table 3: Entrapment efficiency of Phytosomes batches F1-F9

S. No	Formulation Code	Entrapment efficiency (%)
1.	F1	60.45
2.	F2	50.22
3.	F3	76.19
4.	F4	73.62
5.	F5	55.93
6.	F6	69.25
7.	F7	66.47
8.	F8	63.58
9.	F9	79.56

The results of analysis of variance for the Entrapment efficiency (R2) are listed in Table 3. The Entrapment efficiency of phytosomes formulations ranged from 50.22% to 79.56% for the 9 experimental runs. All components of the formulation affected R2. On the basis of these results, the following equation was obtained for the Entrapment efficiency (R2).

Entrapment efficiency= 67.95+5.02A+10.13B+0.0200AB-0.0833A2-2.62B2 4.99A2B+4.52AB2

Above equation showed that the magnitude of the coefficient was in the order B>Aand that B was the most significant component of the phytosomes formulation that affected R2. A higher ratio of B improved the phytosomes characteristics.The relationship between the independent variables on Entrapment Efficiency is schematically illustrated by Contour graph (Figure 3) & a three-dimensional plot (Figure 4).

Particle sizeand Zeta potential:

Particle size of prepared Curcumin phytosomes formulation was determined which was ranged in between 322.85-399.71 nm. Zeta potential of the prepared Curcumin phytosomes was ranged between 42.3-54.9 mV. Results of Particle size and Zeta potential were presented in table 4.14 & 4.15.

Table 4: Particle size of Curcumin phytosomes formulation batches (F1-F9):

S. No	Formulation Code	Particle Size (nm)
1.	F1	399.71
2.	F2	385.25
3.	F3	379.64
4.	F4	363.83
5.	F5	356.48
6.	F6	348.32
7.	F7	341.91
8.	F8	337.53
9.	F9	322.85

Table 5: Zeta potential analysis of Curcumin phytosomes formulation batches (F1-F9):

S. No	Formulation Code	Zeta potential mean (mV)
1.	F1	-54.42
2.	F2	-52.31

3.	F3	-53.54
4.	F4	-51.82
5.	F5	-48.43
6.	F6	-43.59
7.	F7	-47.38
8.	F8	-43.17
9.	F9	-42.11

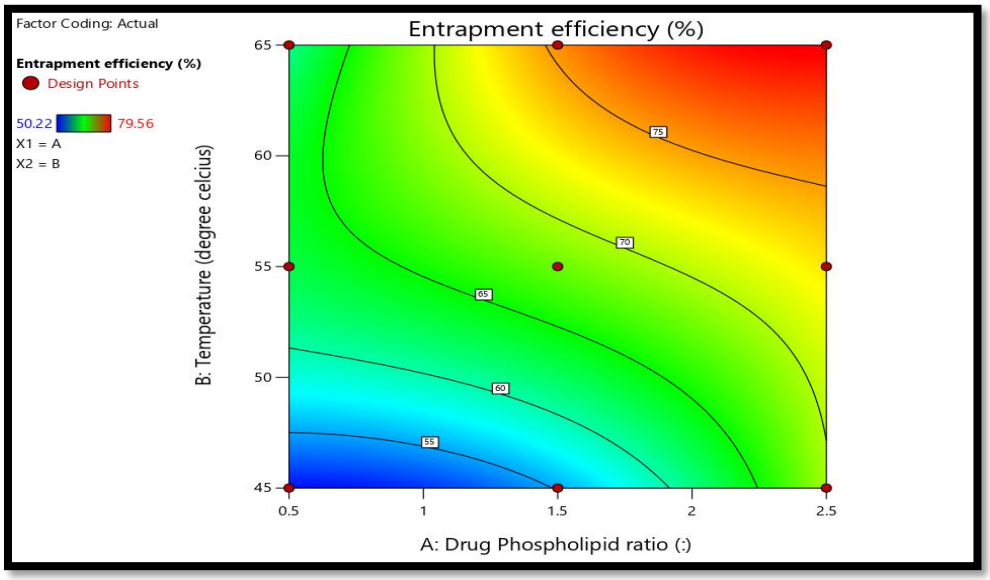

Figure 3: Contour graph showing the effect of Drug phospholipid ratio & Temperature on R2 (Entrapment efficiency)

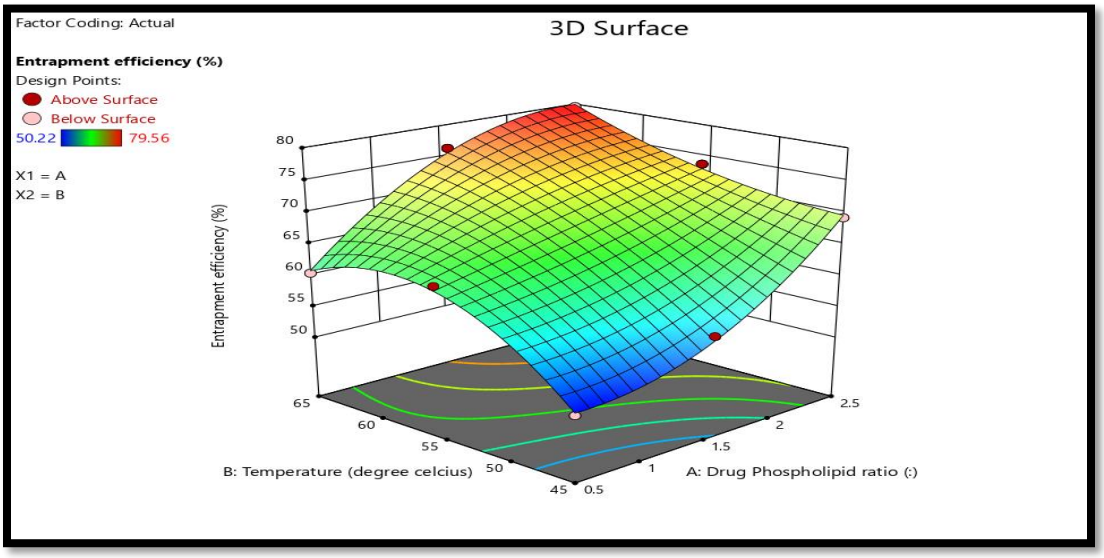

Figure 4: 3D graph showing the effect of Drug phospholipid ratio & Temperature on R2 (Entrapment efficiency)

FT-IR Analysis:

A FT-IR spectrum of Curcumin, Soya lecithin, Physical Mixture of Curcumin & Soya lecithin (1:1) were obtained in the 4000 - 400 cm^{-1} region using FT-IR spectrophotometer in order to get insight into occurrence of interaction between Curcumin and Soya-lecithin.The principal IR absorption peaks of Curcumin at 3507.36cm^{-1} (Phenolic O-H stretching vibration) 1628 cm^{-1} (Aromatic moiety C=C stretching) 1597 cm^{-1} (Benzene ring stretching vibrations) 1509 cm^{-1}(C=O and C=C vibrations)1428cm^{-1} (Olefinic C-H bending vibrations), 1278 cm^{-1} (Aromatic C-O Stretching Vibrations) and 1024cm^{-1} (C-O-C stretching vibrations) was observed in the spectra of Curcumin. The principal IR absorption peaks of Soya lecithin at 2922.86 and 2853.36cm−1 (CH_2 stretching vibration), 1737.40cm−1 (Symmetrical C=O stretching vibration), 1616.12cm−1 (Water scissoring band) and 1234.66cm−1 (PO4 antisymmetric stretching bands) were all observed in the spectra of Soya lecithin.FTIR of Pure drug and physical mixture studies were carried out to eliminate the possibility of interaction between drug and excipients. All the spectrum peaks revealed that corresponding peaks of drugs are present in the above spectra along with excipients peaks.

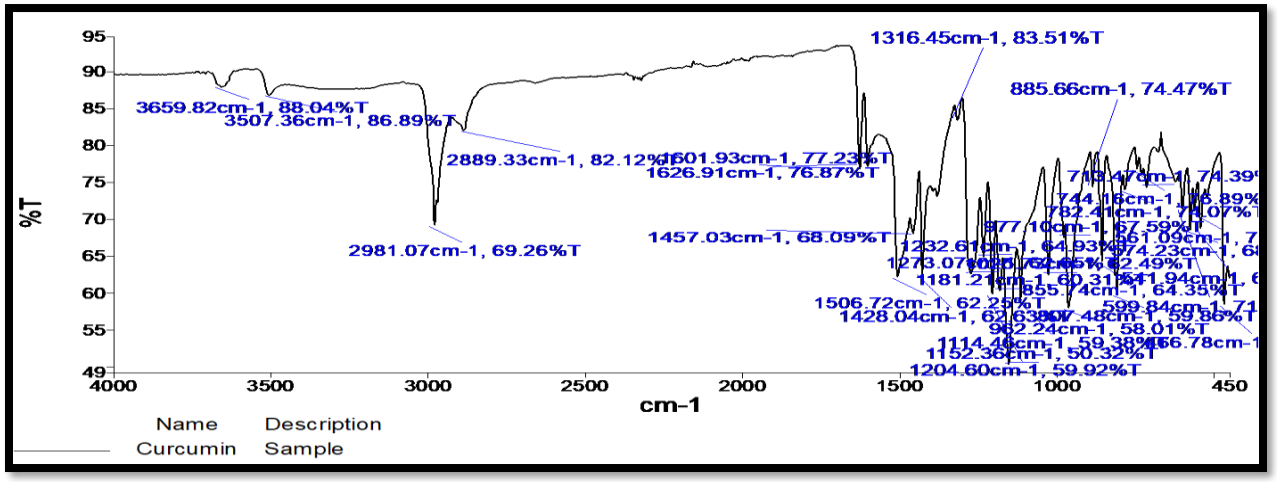

Figure 5: FTIR spectra of Curcumin (pure)

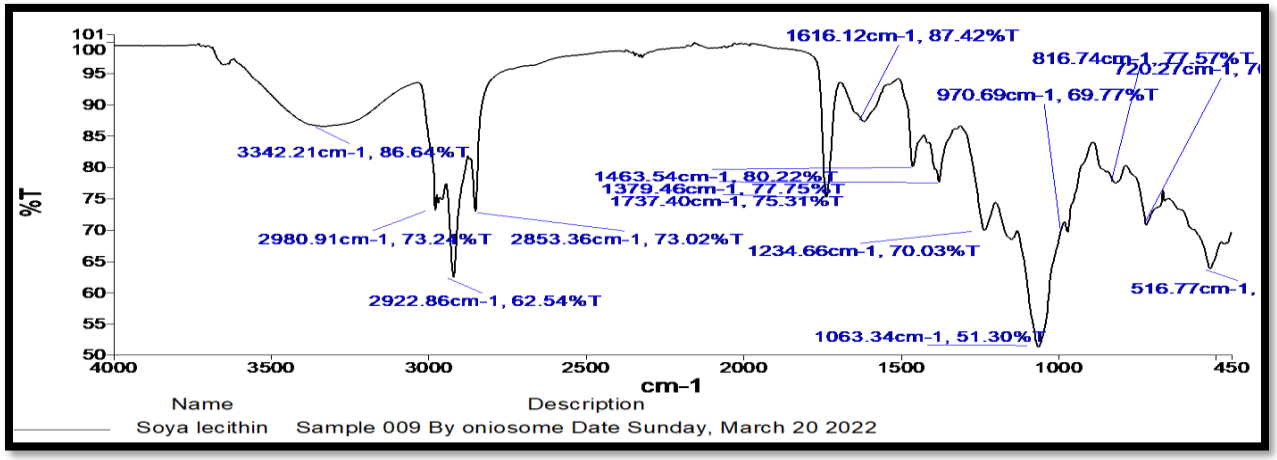

Figure 6: FTIR spectra of Soy lecithin

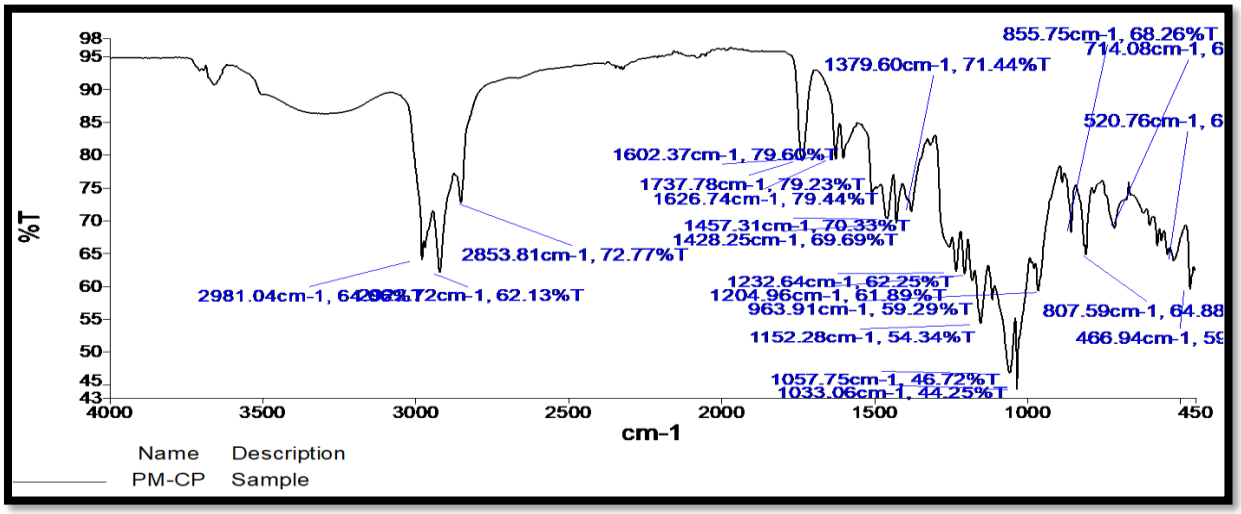

Figure 7: FTIR study of Physical Mixture (Curcumin & Soya lecithin)

Differential scanning calorimetry (DSC):

DSC thermogram of Curcumin in Figure 4.7 demonstrated one broad endothermic peak. The endothermic peak is noticed at 178.95 °C. DSC thermogram of Lipid demonstrate one broad endothermic peak. The endothermic peak is noticed at 156.98 °C.From the physical mixture DSC thermogram of Curcumin & Lipid showed endothermic peak at 178.95 °C with peaks of curcumin & Lipid.

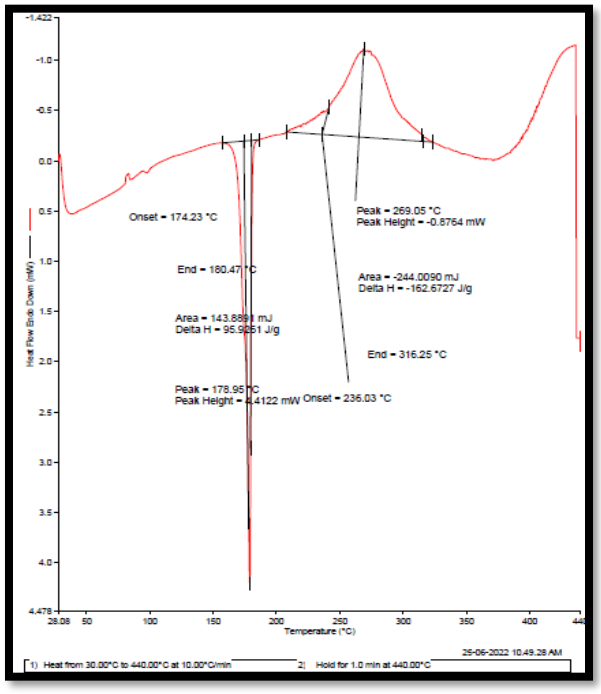

Figure 8: DSC study of Curcumin

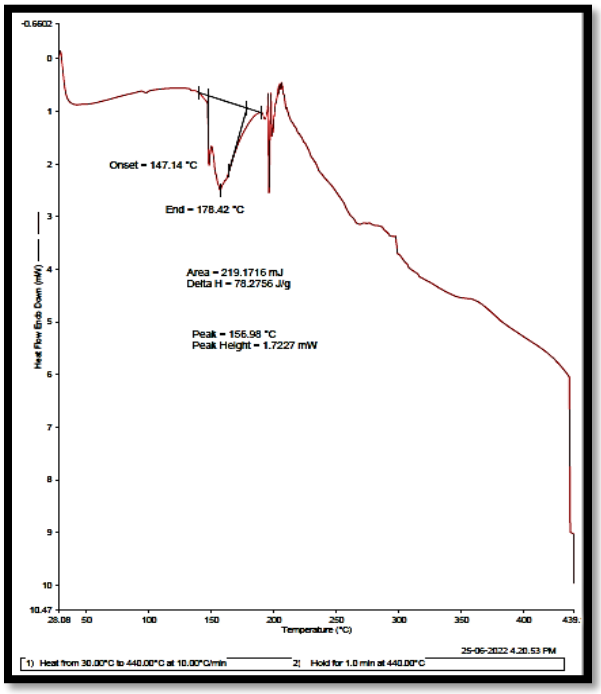

Figure 9: DSC study of Lipid

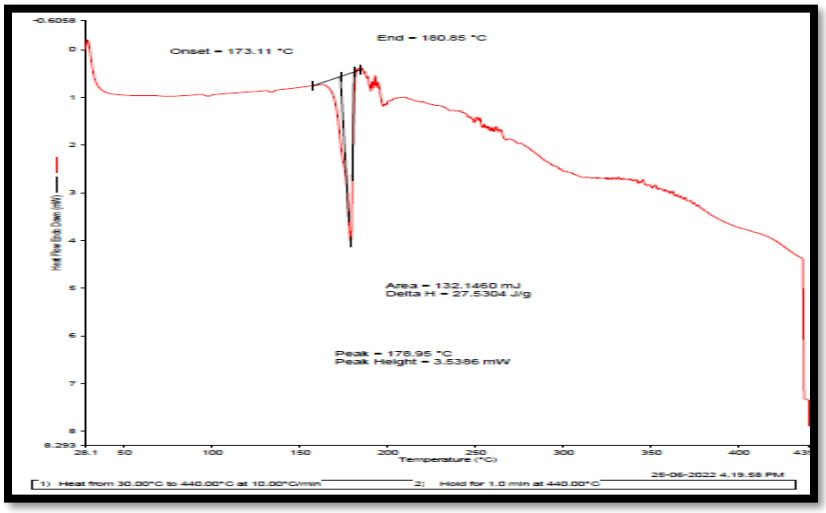

Figure 10: DSC study of Physical Mixture (curcumin & Lipid)

Percentage drug release:

The prepared Curcumin phytosomes were evaluated for in-vitro dissolution study and results are depicted in the table 6.

Table 6: Drug release from Curcumin Phytosomes formulation batches F1-F9

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	12.85	10.52	20.84	16.92	11.96	18.44	15.79	13.15	22.89
2	25.93	22.83	30.68	28.46	24.69	29.37	27.47	26.81	31.65
3	34.41	31.92	39.27	37.28	33.24	38.83	36.52	35.73	41.36
4	43.79	40.75	48.63	46.69	42.86	47.29	45.31	44.55	50.62
5	56.36	54.42	61.91	59.37	55.47	60.46	58.48	57.84	62.84
6	60.21	58.64	65.79	63.46	59.83	64.58	62.83	61.72	66.95
8	64.49	62.17	69.46	67.83	63.79	68.15	66.42	65.25	71.31
10	75.72	72.33	81.37	79.48	74.51	80.56	78.65	76.91	81.83
12	86.74	85.21	89.01	87.92	86.28	88.15	87.59	86.97	90.83

The in-vitro dissolution study revealed that maximum release was found to be minimum (86.74%) from batch F1 and maximum(90.83%) from batch F9 at the end of 12 hr.

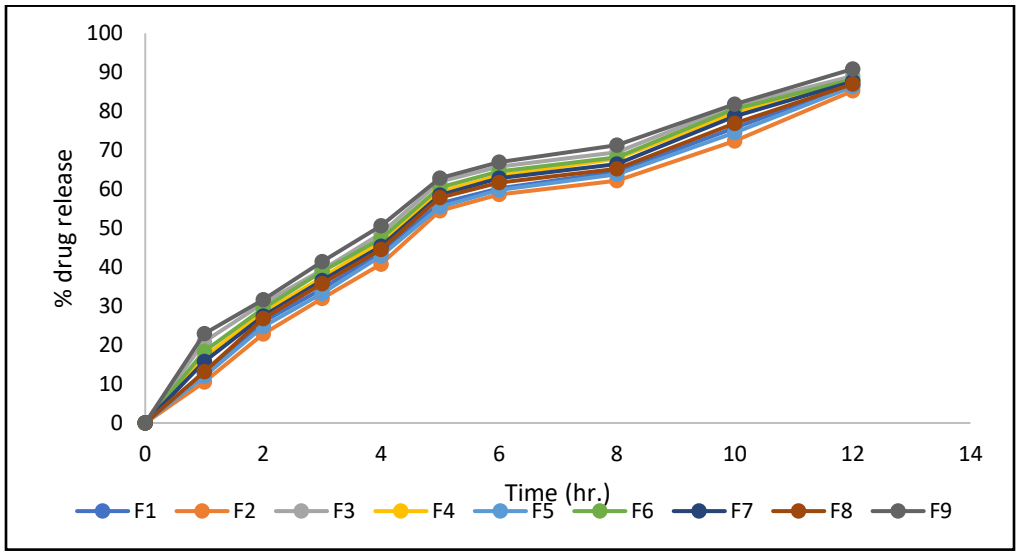

Figure 11: In-vitro dissolution profile of Curcumin phytosomes formulations (F1-F9)

Optimization of Curcumin Phytosomes formulation

Based on the results of evaluation parameters and predicted solution given by the optimization tool, an optimized Curcumin formulation was developed with the most useful properties. The software proposed various suggestions for several combinations of different levels of the factors. The optimum formulation contained 2.382 ratio of factor A (Drug: Phospholipid ratio) and 64.828^0 C of factor B (Temperature). The optimum phytosomes formulation had a practical yield of 88.783%, Entrapment efficiency of 79.775%, and the expected results of the dependent variables of the optimized Curcumin formulation (CU-OPT). Table 7 shows that the experimental and suggested values of the responses of the optimum phytosomes formulation were in line without significant variations ($p > 0.05$), confirming the model's validation and precision (Fig. 4.17).

Table 7: Actual and Experimental Values of the Optimized (CU-OPT) Phytosomes Formulation:

Solution	Drug: Phospholipid ratio	Temperature	Percentage yield	Entrapment Efficiency
Predicted	2.382	64.828	88.783	79.775
Actual	2.382	64.828	88.128	79.615

Checkpoint Analysis

The experimental and expected R^2 values supported the predictive accuracy of the proposed regression models. Further, the ratios of the actual to expected values had a low percentage of error, and there were reasonable residuals between the predicted and experimental responses; this suggests a lack of curvature in the data and adequacy of the model.

Evaluation Parameters for Optimized batch of phytosomes formulation of Curcumin:

Table 8: Evaluation Parameters for Optimized batch (CU-OPT)

S. No	Parameter	Inference
1.	Percent Yield	88.128
2.	Zeta potential	-42.3 mV
3.	Poly dispersity Index	0.120
4.	Particle size (nm)	321.6 nm
5.	Entrapment Efficiency	79.615%
6.	In- vitro drug release	91.77±0.023 %

Scanning electron microscopy

The morphology of the emulsion droplet for the optimized Cur-loaded phytosomes formulation was observed using a scanning electron microscope. The result is depicted in following figure.

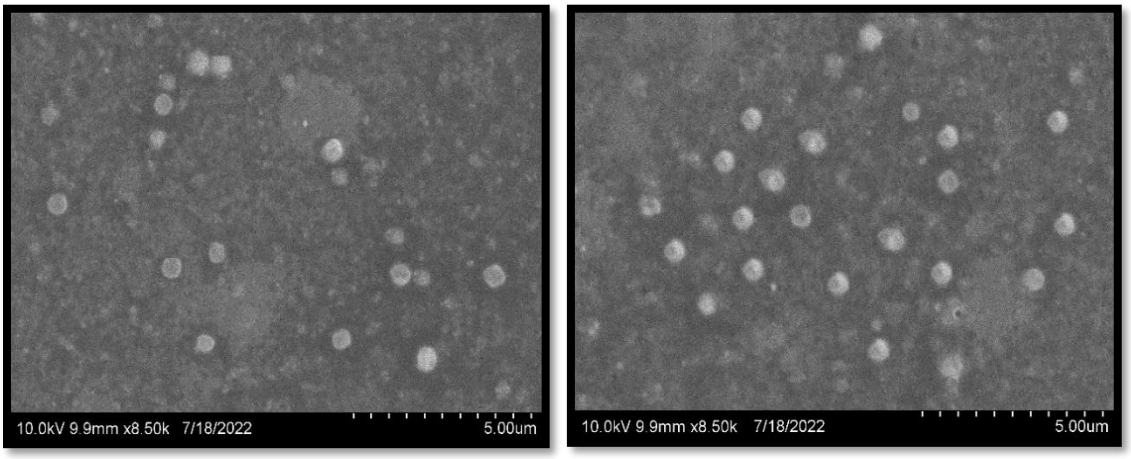

Figure 12:SEM image of the optimized Cur-loaded phytosomes formulation

The SEM study was done to check surface morphology of the drug particles. The SEM of Cur-loaded phytosomes formulation was of round shape and regular size.

CONCLUSION:

Lipid-based vesicular carriers known as phytosomes can be utilized to carry plant-derived nutraceuticals like poly-phenols. A novel phytosomal formulation of Curcumin was developed and evaluated for in-vitro drug release. The complexation of Curcumin with soya lecithin proved successful. The Curcumin loaded phytosomes have homogenous particle size distribution with smaller

sizes. It is because of this that the phytosomes have increased permeability across the intestinal lipid barrier, which results in better bioavailability. To enhance the polyphenol and flavonoids phytocompounds' absorption, bioavailability, safety, and sustained drug release from formulation, the study found an important role for phospholipids in the production of phytosomes. *In-vitro* evaluation parameters i.e., % yield, entrapment efficiency, particle size & zeta potential and *in-vitro* dissolution study showed that the prepared phytosomes were nano-sized having good entrapment efficiency. Furthermore, *in-vitro* release tests showed that our suggested Curcumin-phytosomes released more polyphenol confirming their improved permeability across the intestinal lipid membrane. Thus, the delivery system shows better outcomes and successfully increased bioavailability of plant extract. Further research on optimization, conversion of Curmin-loaded phytosomes in to a suitable dosage form such as gelform and pharmacokinetic characteristics may be helpful to validate the elevated absorption and the improved bioavailability studies.

REFERENCES-

1. Chen, X., Zou, L. Q., Niu, J., Liu, W., Peng, S. F., & Liu, C. M. (2015). The stability, sustained release and cellular antioxidant activity of curcumin nanoliposomes. *Molecules*, *20*(8), 14293-14311.
2. Sharma, V., & Pathak, K. (2016). Effect of hydrogen bond formation/replacement on solubility characteristics, gastric permeation and pharmacokinetics of curcumin by application of powder solution technology. *ActaPharmaceuticaSinica B*, *6*(6), 600-613.
3. Telange, D. R., Patil, A. T., Pethe, A. M., Fegade, H., Anand, S., & Dave, V. S. (2017). Formulation and characterization of an apigenin-phospholipid phytosome (APLC) for improved solubility, in vivo bioavailability, and antioxidant potential. *European Journal of Pharmaceutical Sciences*, *108*, 36-49.
4. Ayuhastuti, A., Agustin, A. N., &Fauziyyah, S. R. (2017). Development of Phytosome-Black Tea Extract Complex By Different Methods And Study Of Cholesterol's Effect On Entrapment Efficiency. *RESEARCH JOURNAL OF PHARMACEUTICAL BIOLOGICAL AND CHEMICAL SCIENCES*, *8*(1), 995-1004.
5. Udapurkar, P. P., Bhusnure, O. G., &Kamble, S. R. (2018). DiosminPhytosomes: development, optimization and physicochemical characterization. *Indian J Pharm Educ Res*, *52*(4), S29-S36.
6. Danaei, M., Dehghankhold, M., Ataei, S., HasanzadehDavarani, F., Javanmard, R., Dokhani, A., ...&Mozafari, M. R. (2018). Impact of particle size and polydispersity index on the clinical applications of lipidicnanocarrier systems. *Pharmaceutics*, *10*(2), 57.
7. Ingebrigtsen, L., &Brandl, M. (2002). Determination of the size distribution of liposomes by SEC fractionation, and PCS analysis and enzymatic assay of lipid content. *AAPS PharmSciTech*, *3*, 9-15.
8. Sonawane, D. D., Jat, R. K., &Pawar, A. Y. (2018). Development of microwave generated Nanocomposites for solubility enhancement of BCS class II drug. *Pharma Innov J*, *7*(12), 270-7.
9. El-Menshawe, S. F.; Ali, A. A.; Rabeh, M. A.; Khalil, N. M. Nanosized Soy Phytosome-Based Thermogel as Topical anti- Obesity Formulation: An Approach for Acceptable Level of

Evidence of an Effective Novel Herbal Weight Loss Product. Int. J. Nanomed. 2018, 13, 307–318. DOI: 10.2147/IJN.S153429.

10. Taleuzzaman, M., Sartaj, A., Kumar Gupta, D., Gilani, S. J., & Mirza, M. A. (2023). Phytosomal gel of Manjistha extract (MJE) formulated and optimized with central composite design of Quality by Design (QbD). *Journal of Dispersion Science and Technology*, *44*(2), 236-244.
11. Sahu, A. R., &Bothara, S. B. (2015). Formulation and evaluation of phytosome drug delivery system of boswelliaserrata extract. *Int J Res Med*, *4*(2), 94-99.
12. Patsariya S.K., Middha Anil., "Antipsoriatic activity of dithranol transdermal proniosomes gel on swiss albino mice", Int. J. Res.Dev.Pharm. L. Sci., 2014, 3(6), pp. 1287-1294.
13. Negi, P., Sharma, I., Hemrajani, C., Rathore, C., Bisht, A., Raza, K., &Katare, O. P. (2019). Thymoquinone-loaded lipid vesicles: a promising nanomedicine for psoriasis. *BMC complementary and alternative medicine*, *19*(1), 1-9.
14. Kumar, S., Singh, K. K., & Rao, R. (2019). Enhanced anti-psoriatic efficacy and regulation of oxidative stress of a novel topical babchi oil (Psoraleacorylifolia) cyclodextrin-based nanogel in a mouse tail model. *Journal of microencapsulation*, *36*(2), 140-155.
15. Kumar, S., Jangir, B. L., & Rao, R. (2022). A new perspective for psoriasis: Dithranolnanosponge loaded hydrogels. *Applied Surface Science Advances*, *12*, 100347.
16. Li, Jing, et al. "A review on phospholipids and their main applications in drug delivery systems." Asian journal of pharmaceutical sciences 10.2 (2015): 81-98.
17. Kumar, Sunil, Minakshi Prasad, and Rekha Rao. "Topical delivery of clobetasol propionate loaded nanosponge hydrogel for effective treatment of psoriasis: Formulation, physicochemical characterization, antipsoriatic potential and biochemical estimation." Materials Science and Engineering: C 119 (2021): 111605.
18. Freitas, Chrysantha, and Rainer H. Müller. "Effect of light and temperature on zeta potential and physical stability in solid lipid nanoparticle (SLN™) dispersions." International journal of pharmaceutics 168.2 (1998): 221-229.
19. Soliman, Ghareb M., Shaaban K. Osman, and Ahmed M. Hamdan. "Preparation and evaluation of anthralin biodegradable nanoparticles as a potential delivery system for the treatment of psoriasisc." International Journal of Pharmacy and Pharmaceutical Sciences 7.12 (2015): 36-40.
20. Dubey, Vaibhav, et al. "Dermal and transdermal delivery of an anti-psoriatic agent via ethanolic liposomes." Journal of controlled release 123.2 (2007): 148-154.
21. 21. 1. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. Indian J of Pharmaceutical Education and Research. 2023;57(3s):s481-s498.
22. Mandal S, Jaiswal DV, Shiva K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. International Journal of Pharmaceutical Research. 2020 Jul;12(3).
23. Bhandari S, Chauhan B, Gupta N, et al. Translational Implications of Neuronal Dopamine D3 Receptors for Preclinical Research and Cns Disorders. African J Biol Sci (South Africa). 2024;6(8):128-140. doi:10.33472/AFJBS.6.8.2024.128-140

24. Tripathi A, Gupta N, Chauhan B, et al. Investigation of the structural and functional properties of starch-g-poly (acrylic acid) hydrogels reinforced with cellulose nanofibers for cu2+ ion adsorption. African J Biol Sci (South Africa). 2024;6(8): 144-153, doi:10.33472/AFJBS.6.8.2024.141-153
25. Mandal S, Bhumika K, Kumar M, Hak J, Vishvakarma P, Sharma UK. A Novel Approach on Micro Sponges Drug Delivery System: Method of Preparations, Application, and its Future Prospective. Indian J of Pharmaceutical Education and Research. 2024;58(1):45-63.
26. Mishra, N., Alagusundaram, M., Sinha, A., Jain, A. V., Kenia, H., Mandal, S., & Sharma, M. (2024). Analytical Method, Development and Validation for Evaluating Repaglinide Efficacy in Type Ii Diabetes Mellitus Management: a Pharmaceutical Perspective. Community Practitioner, 21(2), 29–37. https://doi.org/10.5281/zenodo.10642768
27. Singh, M., Aparna, T. N., Vasanthi, S., Mandal, S., Nemade, L. S., Bali, S., & Kar, N. R. (2024). Enhancement and Evaluation of Soursop (Annona Muricata L.) Leaf Extract in Nanoemulgel: a Comprehensive Study Investigating Its Optimized Formulation and Anti-Acne Potential Against Propionibacterium Acnes, Staphylococcus Aureus, and Staphylococcus Epidermidis Bacteria. Community Practitioner, 21(1), 102–115. https://doi.org/10.5281/zenodo.10570746
28. Khalilullah, H., Balan, P., Jain, A. V., & Mandal, S. (n.d.). Eupatorium Rebaudianum Bertoni (Stevia): Investigating Its Anti-Inflammatory Potential Via Cyclooxygenase and Lipooxygenase Enzyme Inhibition - A Comprehensive Molecular Docking And ADMET. Community Practitioner, 21(03), 118–128. https://doi.org/10.5281/zenodo.10811642
29. Mandal, S. Vishvakarma, P. Pande M.S., Gentamicin Sulphate Based Ophthalmic Nanoemulgel: Formulation and Evaluation, Unravelling A Paradigm Shift in Novel Pharmaceutical Delivery Systems. Community Practitioner, 21(03), 173-211. https://doi.org/10.5281/zenodo.10811540
30. Mandal, S., Tyagi, P., Jain, A. V., & Yadav, P. (n.d.). Advanced Formulation and Comprehensive Pharmacological Evaluation of a Novel Topical Drug Delivery System for the Management and Therapeutic Intervention of Tinea Cruris (Jock Itch). Journal of Nursing, 71(03). https://doi.org/10.5281/zenodo.10811676
31. Mishra, N., Alagusundaram, M., Sinha, A., Jain, A. V., Kenia, H., Mandal, S., & Sharma, M. (2024). Analytical Method, Development and Validation for Evaluating Repaglinide Efficacy in Type Ii Diabetes Mellitus Management: a Pharmaceutical Perspective. Community Practitioner, 21(2), 29–37. https://doi.org/10.5281/zenodo.10642768
32. Singh, M., Aparna, T. N., Vasanthi, S., Mandal, S., Nemade, L. S., Bali, S., & Kar, N. R. (2024). Enhancement and Evaluation of Soursop (Annona Muricata L.) Leaf Extract in Nanoemulgel: a Comprehensive Study Investigating Its Optimized Formulation and Anti-Acne Potential Against Propionibacterium Acnes, Staphylococcus Aureus, and Staphylococcus Epidermidis Bacteria. Community Practitioner, 21(1), 102–115. https://doi.org/10.5281/zenodo.10570746
33. Gupta, N., Negi, P., Joshi, N., Gadipelli, P., Bhumika, K., Aijaz, M., Singhal, P. K., Shami, M., Gupta, A., & Mandal, S. (2024). Assessment of Immunomodulatory Activity in Swiss Albino

Rats Utilizing a Poly-Herbal Formulation: A Comprehensive Study on Immunological Response Modulation. Community Practitioner, 21(3), 553–571. https://doi.org/10.5281/zenodo.10963801

34. Mandal S, Vishvakarma P, Bhumika K. Developments in Emerging Topical Drug Delivery Systems for Ocular Disorders. Curr Drug Res Rev. 2023 Dec 29. doi: 10.2174/0125899775266634231213044704. Epub ahead of print. PMID: 38158868.
35. Abdul Rasheed. A. R, K. Sowmiya, S. N., & Suraj Mandal, Surya Pratap Singh, Habibullah Khallullah, N. P. and D. K. E. (2024). In Silico Docking Analysis of Phytochemical Constituents from Traditional Medicinal Plants: Unveiling Potential Anxiolytic Activity Against Gaba, Community Practitioner, 21(04), 1322–1337. https://doi.org/10.5281/zenodo.1107647136. Tekin, Nilgun Solak, et al. "Nitric oxide levels in patients with psoriasis treated with methotrexate." Mediators of inflammation 2006 (2006).
36. 37. Acharya, N. S., G. V. Parihar, and S. R. Acharya. "Phytosomes: novel approach for delivering herbal extract with improved bioavailability." (2011): 144-160.
37. 38. Sowmya, Cherukuri, et al. "Current trends in treatment and management of psoriasis: an updated review." Int Res J Pharmacy 9.3 (2018): 6-16.
38. 39. Ahmed, Kashif, et al. "Nanoemulsion-and emulsion-based delivery systems for curcumin: Encapsulation and release properties." Food chemistry 132.2 (2012): 799-807.
39. 40. Semalty, Ajay, et al. "Phyto-phospholipid complex of catechin in value added herbal drug delivery." Journal of inclusion phenomena and macrocyclic chemistry 73.1 (2012): 377-386.
40. 41. Yuan, Roufen, et al. "Self-assembled nanoparticles of glycyrrhetic acid-modified pullulan as a novel carrier of curcumin." Molecules 19.9 (2014): 13305-13318.
41. 42. Barry, Jeffrey, et al. "Determining the effects of lipophilic drugs on membrane structure by solid-state NMR spectroscopy: the case of the antioxidant curcumin." Journal of the American Chemical Society 131.12 (2009): 4490-4498.