*ejpmr, 2021,8(11), 716-721*

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

# FORMULATION AND EVALUATION OF CAPSULES CONTAINING PHYYTOSOMES OF *PHYSALIS MINIMA* LINN. FOR IMPROVED THERAPEUTIC OUTCOME

**Nilakshi G. Mahakalkar[1*], Neelam Dighe[2] and Dr. Jasmine G. Avari[3]**

Department of Pharmaceutical Sciences, R.T.M.N.U, Nagpur-440033(MS), India.

***Corresponding Author: Nilakshi G. Mahakalkar**

Department of Pharmaceutical Sciences, R.T.M.N.U, Nagpur-440033(MS), India.

**Article Received on 21/09/2021** **Article Revised on 11/10/2021** **Article Accepted on 31/10/2021**

## ABSTRACT

Herbal drug having some limitation over oral drug delivery which includes poor solubility, permeation and bioavailability so as to improve these parameters of herbal novel drug delivery system known as phytosome is used. By applying this novel approach bioavailability is increased. The objective of the current project is to develop a herbal capsules loaded with phytosomes with a systematic approach to yield better products stability and it can be easily administered with oral drug delivery. It can improved acceptability and therapeutic potential owing to its greater bioavailability. Different phytosomal complexes of *Physalis minima* extracts containing a molar ratio of 1:1, 1:2, 1:4 using methanolic extract and soya lecithin were prepared by solvent evaporatiion technique. *Physalis minima* phytosomes were characterized by particle size, zeta potential, entrapment efficiency, Fourier transform infrared spectroscopy and *in-vitro* drug release. Prepared phytosomes showed 51 % entrapment efficiency, particle size (254nm), zeta potential (-7.57) and field emission scanning electron microscopy (FE-SEM) show spherical shaped particles. *Physalis minima* phytosome loaded capsule showed the capsules weight variation within the limit, disintegration time 10-13 min and *in-vitro* drug release of 93%. The drug content was found to be in the range of 69-83 % in all formulations.

**KEYWORDS:** Phytosomes, novel drug delivery, entrapment efficiency.

## INTRODUCTION

The drugs of traditional ayurvedic origin can be utilized in a advanced form with enhanced efficacy by incorporating in modern dosage forms. However, phototherapeutics need a modern technology approach to deliver the components in a new manner to increase patient compliance and decreasing dose frequency. This can be achieved by designing novel drug delivery systems for herbal extracts. Novel drug delivery systems reduce the dose frequency to overcome patient non-compliance, but also increase the therapeutic value by reducing toxicity and increasing the bioavailability.[1-2]

*Physalis minima* Linn belonging to Solanaceae family. *P. minima* is an annual herb found throughout India, Baluchistan, Afghanistan, Tropical Africa and Australia and is reported as one of the important medicinal plants in Indian Traditional System of Medicines. The plant majorly contains phenolics, alkaloids, steroids and flavonoids. The presence of phenolics and alkaloids in large amount suggest that the plants having various pharmacological action like antioxidant, anti-cancerous, anti-diabetic, analgesic, antipyretic and anti-inflammatory potentials.[3-5]

Herbal extracts have many compounds which degraded in the highly acidic pH of the stomach. Other ingredients could be metabolized in first pass metabolism before reaching the systemic circulation. In addition, herbal extracts are often poorly compressible and very hygroscopic powders showing poor powder flowability. As herbal drugs have much potential, several researchers are trying to develop novel drug delivery systems, such as solid dispersion, nanoparticles, fast-dissolving tablets, sustained release formulations, microparticles, microcapsules and mucoadhesive systems. Phytosomse are newly structured molecule of herbal constituent surrounded by phospholipid which having water soluble heads and lipid soluble tails. Phytosomes formulation show better pharmacokinetic and pharmacodynamic profile than conventional herbal extracts because of its ampliphilic nature Oral herbal drug delivery with novel approach of nanotechnology is the best to increase herbal potential and patient compliance and reduce dose frequency.[6-12]

## MATERIAL AND METHODS

Lactose, Magnesium stearate, talc, starch, Sodium starch glycolate was procured from Hi Media Ltd, Mumbai. Capsules shell procured from Snehal pharmaceuticals. Plant of *Physalis minima* Linn. was collected from farm of Wardha in Maharashtra (India) and plant was authenticated by the Department of Pharmacognosy, Pharmaceutical Sciences, R.T.M. Nagpur University,

Nagpur. All the chemicals and reagents used in this study were of analytical grade.

**Extraction of plant**

The whole plant of *Physalis minima* (PM) was shade dried and then grinds into coarse powder with the help of a suitable grinder. The dried plant material then extracted with different solvents according to their polarities petroleum ether, trichloromethane, ethyl acetate, ethanol, methanol by Soxhlet extraction method for 72 hours. Then the semisolid extract freeze dried and store in amber colored glass bottle for further use. Phytochemical screening was carried out for identification of chemical groups present in methanolic extract of *Physalis minima* Linn. using standard procedure.

**Characterization of powdered drug *Physalis minima* Linn.**

**Solubilty of** *Physalis minima* Linn.

Solubility of PM was observed in different solvents like water, ethanol, methanol, DMSO, phosphate buffer (6.8).

**Compatability study**

The FTIR spectrum of PM was measured using Shimadzu IR Affinity- 1S FTIR. The drug sample and phospholipid (PC) were triturated and mixed with potassium bromide in the ratio 1:100. The mixture was then introduced in the sample holder of the FT-IR instrument and was scanned to obtain spectra in range from 4000 to 400 cm-1. FTIR spectrum obtained for the mixture of plant and PC compared with the PM to determine any interaction between them.

**Determination maximum wavelength and standard calibration curve in phosphate buffer**

Ultraviolet spectrophotometric method was carried out using phosphate buffer (pH 6.8) as solvent media. *Physalis minima* extract solution in phosphate buffer (pH 6.8) was scanned between 200-800 UV-Visible range for obtaining absorbance maxima. Then the absorbance of the different serial dilution (20-120ppm) samples was measured at the λ max using a UV spectrophotometer (V-630, Jasco) and a standard calibration curve was plotted with concentration against absorbance.

**Preparation and Characterization of Phytosomes**

Phytosomes were prepared by solvent evaporation method. Herbal extract and phosphotidylcholine (1:1, 1:2, 1:3) dissolve in 50 ml of dichloromethane with varying stirring time(30-90 min) in the beaker at $40^0$C. Then semisolid complex dried in rotary evaporator until thin film formation and film hydrate with 20 ml of n-hexane with continuous stirring to form precipitate. Then precipitated complex filtered and dried under vacuum to remove the traces of solvent. The obtained phytosomal formulations (P1-P9) were stored in amber colored glass bottle in refrigerator.

Prepared phytosomes evaluated for % entrapment efficiency, particle size, PDI, zeta potential and field emission scanning electron microscopy (FE-SEM).

**Formulation of herbal hard gelatin capsules**

Accurately weighed 250 mg *physalis minima* phytosomes was mixed with lactose monohydrate, talc and magnesium stearate by trituration method. After trituration, blend was passed through sieve. The fine powder was collected and filled in capsule shell (#1) using hand operated capsule filling machine. The composition of herbal capsules was recorded in Table 1.

**Table no. 1: Composition of phytosomes loaded hard gelatin capsule.**

| Content | Quantity |
|---|---|
| *Physalis minima* phytosomes | 250 mg |
| Lactose monohydrate | 126 mg |
| Talc | 12 mg |
| Magnesium Stearate | 12mg |
| **Total net weight of capsule** | **400mg** |

**Evaluation herbal capsule**

**Estimation of drug content in capsules**

Powder from 10 capsules were mixed and weight of powder equivalent to 10 mg of *physalis minima* and extracted with the phosphate buffer of pH 6.8 for 30 min. These solutions were filtered, suitably diluted and absorbance was measured at 273nm against blank solution (phosphate buffer pH 6.8) using a UV spectrophotometer.

**Determination of uniformity of weight**

Twenty capsules were selected. Each capsule was weighed on electronic balance, emptied of its content, the shells reweighed and the weight of content determined. The collective weight of content, average weight of content per capsule and the deviations (%) of individual content weights from the mean were calculated.

**Determination of disintegration time**

Disintegration times for capsules were determined by disintegration apparatus. Six capsules were placed in six tubes of the basket and the apparatus was operated using water as release medium maintained at 37 ± 2°C. The capsules were observed and the times taken for complete disintegration of all capsules were determined.

***In-vitro* dissolution study of capsules**

*In-vitro* dissolution study of all the prepared capsule formulations was done using USP Type II paddle dissolution apparatus using 900 ml phosphate buffer pH 6.8 at 100 rpm. An aliquot amount of the sample was withdrawn at regular time intervals and the same volume of pre-warmed (37±0.5ºC) fresh dissolution medium was replaced. The samples were filtered, suitably diluted and it was analyzed by using Shimadzu UV-spectrophotometer at 273 nm**.**

## RESULTS AND DISCUSSIONS

**Solubilty of** *Physalis minima* Linn.

Solubility of *Physalis minima* Linn. was found to be soluble in methanol, ethanol, DMSO, phosphate buffer.

**Compatibility study**

The compatibility study between PM and PC occurs due to the formation of the complex can be confirmed by the FT-IR spectroscopy comparing the spectrum of the complex with the spectrum of individual components and their physical mixtures. FTIR spectra showed the changes in peaks in complexes and positions from that of PM and PC. PM showed the characteristic IR peaks and PC complex shows the disappearance of alkene C=C indicates that phospholipid has interacted with PM in the process of complexation shown in figure no 1. The appearance of S=O of broad peak shows the complexation between PC and PM that sustains in the physical mixture. On the other hand, the physical mixture showed the disappearance of amine group N-H that showed in the complexation while it shows all the sharp peaks at about the same positions as that of PM.

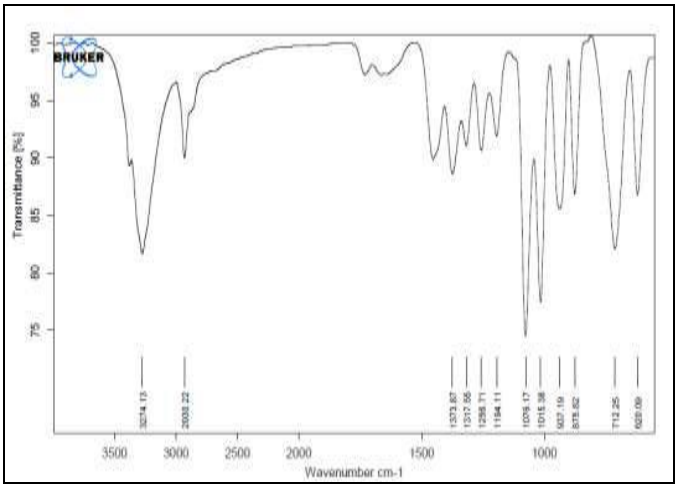


**Figure no 1: FT-IR spectrum of Phospholipid and PM.**

**Determination maximum wavelength and standard calibration curve in phosphate buffer**

The maximum wavelength of concentration 100mcg/ml of PM in phosphate buffer 6.8 was found to be 273 nm shown in figure no 2. The standard curve at 273 nm showed the linearity. The plotted graph absorbance against concentration shows that it follows Beer-Lambert's law with regression value (R2) of 0.9942 show in figure no.3.

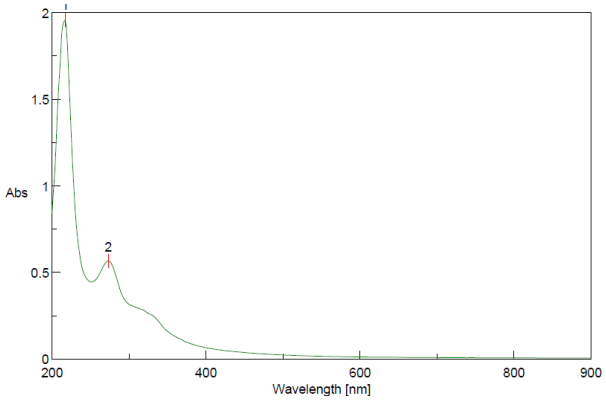


**Figure no.2: UV spectrum of PM in pH 6.8 buffer.**

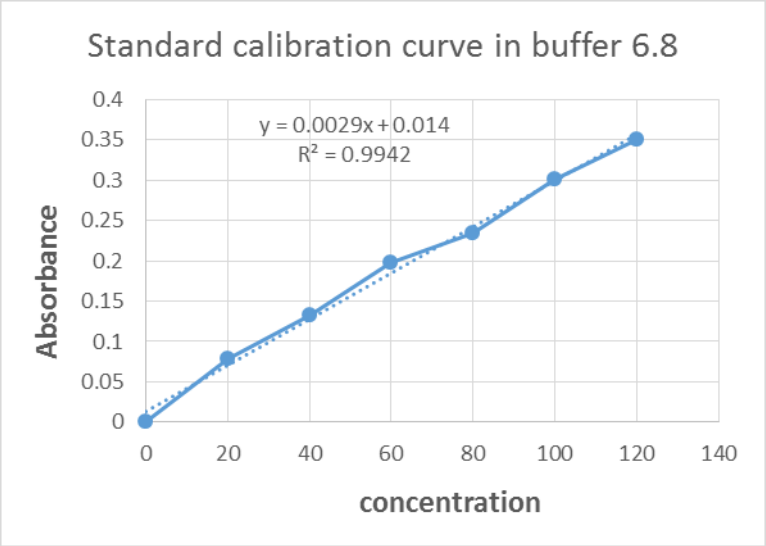


**Figure no.3: Standard calibration curve in Phosphate buffer 6.8 at 273 nm.**

**Preparation and Characterization of Phytosomes**

Phytosomal formulations (P1-P9) were prepared successfully by solvent evaporation method. Optimized phytosomal formulation (P3) showed 51% entrapment efficiency, particle size (254nm), PDI, zeta potential (-7.57) and field emission scanning electron microscopy (FE-SEM).

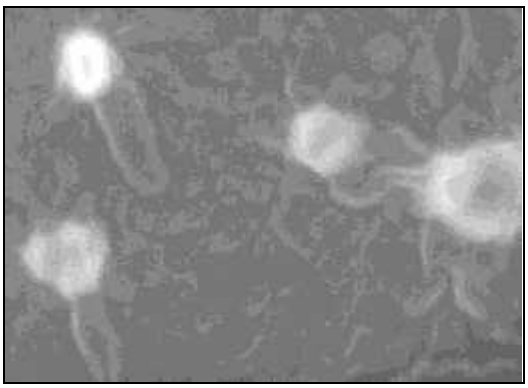

**Figure no. 4: FE-SEM image of phytosomes.**

**Formulation of herbal hard gelatin capsules**

Accurately weighed 250 mg *physalis minima* phytosomes with required quantity of excipients were filled in 30 capsules shell (#1) using hand operated capsule filling machine.

**Evaluation herbal capsule**

All the capsules tested for weight variation falls within the acceptable standard limit given for the weight variation. The drug content was found to be in the range of 69-83% in all formulations. All the formulation show the disintegration time in the range of 10-13 min.

***In-vitro* dissolution study of capsules**

*Physalis minima* phytosome loaded capsule showed the release of 93%. The drug release data of the *in-vitro* drug release study was analyzed with various kinetic models like zero order, first order, Higuchi model, Korsmeyer-Peppas model. The correlation values were calculated for the linear curves by regression analysis of the plots. The drug release by diffusion mechanism at a comparatively slower rate with increase in time can be related linearly to % drug release. To confirm the drug release diffusion mechanism, data was fitted in the Korsmeyer-Peppas model. The regression coefficient was found to be highest in the Korsmeyer-Peppas model with the value of R2= 0.9674 and n value was found to be 0.6781 which is nearer to 1 indicating Non-Fickian type so it confirmed that drug release follows both diffusion and erosion mechanism.

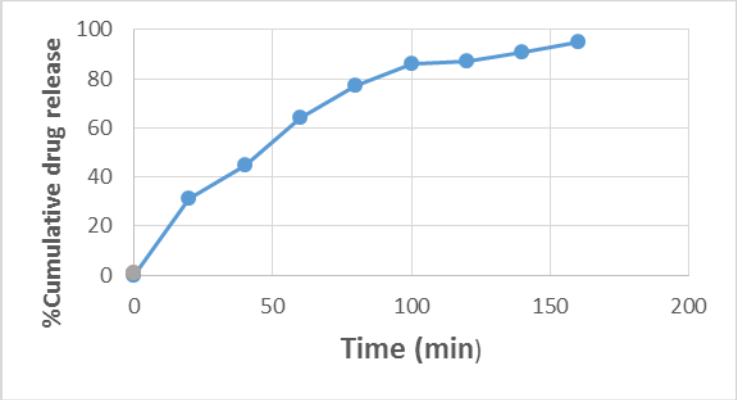


**Figure no. 5: *In-vitro* dissolution studies of herbal capsule.**

## CONCLUSION

Herbal extract having various solubility, permeation and bioavailability limitations which can affect their therapeutic effect. From the study it can be concluded phytosomes is the novel nanotechnology formulation containing lipid which can form complex with extract and improve their efficacy by improve their particle size and permeation. It can also conclude that phytosomes are more bioavailable than conventional herbal extract of *Physalis minima* Linn. owing to their enhanced capacity to cross lipid rich biomembranes by overcome pharmacokinetic variance and it can be delivered easily with oral route in form of herbal capsules.

## AKNOWLEDGEMENT

The authors gratefully acknowledge Department of Pharmaceutical Sciences RTM Nagpur University, Nagpur to provide all laboratory facilities for research work. We also thankful to Department of Pharmacognosy, RTM Nagpur University, Nagpur to identified the plant.

## REFERENCES

1. Garima Jain, Umesh Patil, 2015. "Strategies for enhancement of bioavailability of medicinal agents with natural products", International Journal of Pharmaceutical Sciences and Research, 6(12): 5315-24.
2. Tatsushi Mutoh, Tomoko Mutoh, Yasuyuki Taki, Tatsuya Ishikawa, 2016. "Therapeutic potential of natural product based oral nanomedicines for stroke prevention", Journal of Medicinal Food, 19(6): 521-527.
3. Daya Chothani, H. Waghasiya, 2012. "Indian A phyto-pharmacological ovreview on *Physalis minima* Linn.", Indian journal of Natural Products and Resources, 3(4): 477-482.
4. Venkanna Banothu, Uma Adepally, Jayalxmi Lingam, 2017. "In-vitro total phenolics, flavonoids contents, antioxidant and antimicrobial activities of various solvents extracts from the medicinal plant *Physalis minima* Linn." International Journal of Pharmacy and Pharmaceutical Sciences, 9(3): 192-198.
5. Dibyendu Shil, Damiki Laloo, Smriti Rekha Chanda Das, Suvakanta Dash, 2019. "Pharmacognostical and phytochemical standardization of *Physalis minima* Linn leaf" International Journal of Pharmacy and Pharmaceutical Sciences, 11(11): 20-25.
6. Bui Thanh Tung, Nguyen Thanh Hai, Phan Ke Son, 2017. "Hepatoprotective effect of Phytosome Curcumin against paracetamol-induced liver toxicity in mice", Brazilian Journal of Pharmaceutical Sciences, 53(1): 1-13.
7. Patel Amit, Tanwar Y.S., Suman Rakesh, Patel poojan, 2013. "Phytosome: Phytolipid Drug Dilivery System for Improving Bioavailability of Herbal Drug", Journal of Pharmaceutical Sciences and Bioscintific Research, 3(2): 51-57.
8. Arun Kumar, Bimlesh Kumar, Sachin Kumar Singh, Barinder Kaur, Saurabh Singh, 2017. "A review on phytosomes: novel approach for herbal phytochemicals", Asian Journal of Pharmaceutical and Clinical Research, 10(10): 41-47.
9. Bhuwanendra Singh, Rajendra Awasthi, Arshad Ahmad, Asif Saifi, 2018. "Phytosome: most significant tool for herbal drug delivery to enhance the therapeutic benefits of phytoconstituents", 8(1): 98-102.
10. Pande S. D., Wagh A.S., Bhagure L.B., Patil S.G., Deshmukh A.R., 2015. "Preparation and Evaluation of Phytosomes of Pomegrane Peels" Research Journal of Pharmacy and Technology, 8(4): 416-422.
11. P R Thurapati, S M Reddy, 2011. "Phytosomes: Novel Phytophospholipid carriers for herbal drug delivery", International Journal of Health Research. 2(6): 28-33.
12. Parul Ittadwar, Prashant Puranik, 2017. "Novel umbelliferone phytosomes: Development and optimization using experimental design approach and evaluation of photo-protective and antioxidant activitry", International Journal of Pharmacy and Pharmaceutical Sciences, 9(1): 218-228.
13. Soni HK, Ribadiya NC, Bhatt SB, Sheth N. Evaluation of herbal formulation (capsule) containing Ashwagandha as a single herb with their nutritional value determination. Int J Appl Biol Pharm Tech., 2010; 1(3): 960-967.

14. Ranjana, Mishra A, Mishra A, Gupta R. Determination of gallic acid and β-sitosterol in polyherbal formulation by HPTLC. Pharm Pharmacol Int J., 2016; 4(4): 81-87.
15. Dipak P, Mayank P, Hitesh M, Shah DR, Shrikant J, Bhavin V. Phytochemical screening and standardization of polyherbal formulation "RIPARE" for arthritis. Int J Pharma Res Rev., 2013; 2(6): 29-35.
16. Mohapatra P, Shirwaikara A, Aswatharam HN. Standardization of a polyherbal formulation. Phcog Mag., 2008; 4(13): 65-69.
17. Anita S, Anil W. Formulation and evaluation of polyherbal capsules for antidiabetic activity. World J Pharm Pharm Sci., 2015; 4(8): 1796 – 1801.
18. Akanksha Y, Atul KS, Singh AK, Gautam SS, Raj KP. Formulation and evaluation of hard vegetable capsule for healthy brain using powder of green tea and Brahmi extract. Int J Pharm Pharm Res., 2016; 6(1): 7-21.
19. Nayeemullah KM, Suresh J, Hemant YKS, Ahuja J. Formulation and evaluation of antistress polyherbal capsule. Der Pharmacia Sinica, 2012; 3(2): 177-184.
20. Shaukat M, Ghazala HR, Huma S, Shahnaz G, Sumaira I, Rehana P. Development of standardized formulation of monoherbal (250mg) capsule. Int J Herbal Med., 2013; 1(4): 44-49.
21. Harshika A, Dayanandan M, Rajendra N, Anuradha N, Kauser U, Sanjay K. Standardization, preparation and evaluation of an Ayurvedic polyherbal formulation in capsule dosage form suitable for use in clinical trials. Indo American J Pharma Res., 2014; 4(10): 4093-4099.