Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 5, 2026

# Development and Evaluation of Herbal Based Drug Delivery System for Management of Metabolism Disorder

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## ABSTRACT

The aim of the study was development and evaluation of herbal based drug delivery system for management of metabolism disorder. Fresh leaves of *Gymnema sylvestre* were collected from the Kanpur region, Uttar Pradesh. Leaves were washed and dried under shade and authenticated by the Botanist. The leaves of *Gymnema sylvestre* were soaked in a beaker containing distilled water and ethanol (1:1) solvent system for 15 days with gradual stirrings (cold maceration). The Phytosomes of leaves extract of *Gymnema sylvestre* were developed through Rotary evaporation method. After pre-formulation studies, phytosomes of leaves extract of *Gymnema sylvestre* were characterized for following parameters i.e., physical appearance, solubility, droplet size, polydispersity index, entrapment efficiency, SEM Analysis, *In-vitro* drug release and stability studies. Phytosomes were observed as homogenous and brown in color. After 12 hour, *in-vitro* drug release was estimated as 93.17±0.4, 94.24±0.4, 95.39±0.1 and 94.26±0.2 in F1, F2, F3 and F4. At 800µg/ml, the α-Amylase inhibition was estimated as 72.23±0.07 %, and 94.45±0.11 %, in Phytosome (F3) and acarbose, respectively. It concludes that *Gymnema sylvestre* phytosomes (F3) was most prominent phytosomes among all the phytosome subtypes. It also demonstrated a better stability that can be kept for a month without change in its physical appearance, entrapment and *in-vitro* drug release. Development of *Gymnema sylvestre* phytosomes (F3) might be very significant in terms of managing diabetes mellitus and associated symptoms as well. It can counter the insulin de-sensitivity by facilitating the insulin sensitivity to its binding receptors (Tyrosine kinase).

**Keywords:** *Gymnema sylvestre,* soya lecithin, phytosome, α-Amylase inhibition.

## INTRODUCTION

DM is a metabolic disorder characterized by abnormally high amounts of glucose in the blood. The primary subcategories of DM are Type 1 and Type 2 which typically arise from impaired insulin production and/or function. Type 1 typically occurs in children or teenagers, whereas type 2 diabetes mellitus is commonly seen in middle-aged and older adults who have experienced long-term high blood sugar levels as a result of unhealthy lifestyle and dietary habits (Sapra and Bhandari, 2023). On a global scale, approximately 1 in 11 persons are

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affected by diabetes mellitus, with 90% of them having type 2 DM (Tuomilehto, 2013). The prevalence of Type 1 DM has been steadily rising on a global scale. T1DM rates in the United States have experienced an annual increase of approximately 2% across various age and ethnic groups, with higher prevalence observed among Hispanic kids. The precise cause of this pattern remains undisclosed (Rush et al. 2018).

**Plant profile**

In India *Gymnema sylvestre* (GS) popular traditional medicinal plant for diabetes since, 2000 years. Primarily it was applied for type 2 DM,a state for it is suggested continuously in India. GS belongs to family Asclepiadaceae, commonly called as "gurmar" i.e., sugar destroyer, is a famous plant traditional system of medicine (Pothuraju et al. 2014).

**Fig 1. *Gymnema sylvestre* shrub**

Antidiabetic property is due to the presence of Gymnemic acid. It is also served as sugar making agent, anti-inflammatory value. Antidiabetic novel agent gymnemic acids isolated from the fresh leaves of *G. sylvestre*. Followed by the SAR of the gymnemic acids and other major phytoconstituents of *G. sylvestre* were studied in detailed and elucidated (Khan et al., 2019).

**Taxonomy**

| | |
|---|---|
| Kingdom | Plantae |
| Order | Gentianales |
| Family | Apocynaceae |
| Genus | *Gymnema* |
| Species | *sylvestre* |

*G. sylvestre* leaves are rich source of saponins (triterpene) resembles to oleanane and dammarane. Saponins Oleanane k/a are gymnemic acids and gymnemasaponins, whereas saponins dammarane are gymnemasides principally gymnemic acid A-D, stigmasterol and β-amyrin related glycosides. Other important agents such as anthraquinones, flavones, pentatriacontane, hentri-acontane, phytin, chlorophylls, resins, tartaric acid, *d*-quercitol, butyric acid, formic acid, lupeol and alkaloids. Leaves contains acidic glycosides, anthraquinones and its derivatives (Kritikar,1998).

The aim of study was based on the development and evaluation of herbal based drug delivery system for management of metabolism disorder.

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## MATERIALS AND METHODS

### Chemicals and Instruments

Leaves of *Gymnema sylvestre*, soya lecithin, ethanol, phosphate buffered solution soya lecithin, and distilled water.

Digital weighing balance, Digital pH meter, Franz diffusion cell and UV-Spectrophotometer.

### Collection, and authentication of plant materials

Fresh leaves of *Gymnema sylvestre* were collected from the Kanpur region, Uttar Pradesh. Leaves were washed and dried under shade and authenticated by the Botanist.

### Extraction process

The leaves of *Gymnema sylvestre* were soaked in a beaker containing distilled water and ethanol (1:1) solvent system for 15 days with gradual stirrings (cold maceration). The beaker was mounted with aluminium foil. After the due time, beaker's aluminium foil was removed and filtered using the Whatman filter paper. The obtained slurry was made concentrated through rotatory evaporator. Thus, herbal extracts are available in powder form and weighed to calculate the % yield. All the extracts were kept in desiccator to keep the extract moisture free (Khan et al. 2020).

### Pre-formulation study

### Organoleptic properties

The obtained leaves extract of *Gymnema sylvestre* are observed for their physical characteristics like colour, odour, texture of drug and compared with as reported in official monograph.

### Solubility

The solubility of leaves extract of *Gymnema sylvestre* is determined by placing a small quantity of polymers (about 1-2 mg) individually in a test tube, adding 5ml of solvent (water, ethanol, methanol, phosphate buffer), shaking vigorously, and holding for a while. Take note of the product's solubility in various solvents when it is at room temperature.

### Preparation of standard calibration curve of herbal extracts

100mg of leaves extract of *Gymnema sylvestre* accurately weighed and dissolved in methanol (2ml) and volume was made up to 100ml with 0.1N HCl solution thus stock solution is prepared. The 10ml of stock solution was further diluted with 0.1 N HCl (pH 1.2) in 100ml to get 100µg/ml concentration solution. Then 0.2, 0.4, 0.6, 0.8, and 1ml of solution was taken in 10ml standard volumetric flask and made the volume up to 10 ml with 0.1N HCl to prepare 2µg, 4µg, 6µg, 8µg, and 10µg/ml solution. Then the absorbance was measured in a UV spectrophotometer at 270 nm against 0.1 N HCl as blank. The procedure was repeated with phosphate buffer at pH 6.8 and absorbance is measured at wavelength 270 nm (Reddy et al. 2019).

### Formulation of Phytosomes (Rotary Evaporation method)

The specific amount of leaves extract of *Gymnema sylvestre* and soya lecithin was dissolved in 30 ml of tetrahydrofuran in a rotary round bottom flask followed by stirring for 3 hours at a temperature not exceeding 40ºC. Thin film of the sample was obtained to which n-hexane is

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added and continuously stirred using a magnetic stirrer. The precipitate was collected, placed in amber colored glass bottle and stored at room temperature (Khan et al. 2013).

**Table 1. List of compositions for *Gymnema sylvestre* Phytosomes**

| Formulation | Molar ratio | Drug | Phospholipid | Solvent |
|---|---|---|---|---|
| F1 | 1:1 | *Gymnema sylvestre* | Soya lecithin | Dichloromethane + n-hexane |
| F2 | 1:2 | *Gymnema sylvestre* | Soya lecithin | Dichloromethane + n-hexane |
| F3 | 2:1 | *Gymnema sylvestre* | Soya lecithin | Dichloromethane + n-hexane |
| F4 | 2:2 | *Gymnema sylvestre* | Soya lecithin | Dichloromethane + n-hexane |

## Characterization parameters

### Physical appearance

The formulated phytosomes of leaves extract of *Gymnema sylvestre* were determined for the physical appearances i.e., color, odor, and texture/shape.

### Solubility

The solubility of the phytosomes were estimated in different solvent systems including ethanol, methanol, water, and phosphate buffer solution.

### Particle size & Polydispersity index analysis

Zetasizer Nano-ZS was used to measure the average particle size of the phytosome. The measurements were taken at a 90º angle at 25ºC. To make sure the light scattering intensity was within the instrument sensitivity range, methanol was used to dilute the phytosomes. All measurements were made at 25c. The same instrument is used to calculate the formulation's polydispersity index. The polydispersity index revealed the width of the size distribution (Samadhan et al. 2019).

### Entrapment efficiency

Phytosome complex of leaves extract of *Gymnema sylvestre* is diluted 1-fold with 10 ml of methanol and then centrifuged at 18,000 rpm for 1/2 h at -4oC using cooling centrifuge machine. The supernatant was isolated and the amount of free leaves extract of *Gymnema sylvestre* is determined by UV/Vis. spectroscopy at 269nm. To determine the total amount of leaves extract of *Gymnema sylvestre*, 0.1 ml of the leaves extract of *Gymnema sylvestre* phospholipid suspension was diluted in methanol, adjusting the volume to 10 ml (Habbu et al. 2013).

Entrapment efficiency: Total amount- Free amount/ Total amount × 100

### DSC analysis

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*Gymnema sylvestre,* soya lecithin phospholipids, physical mixture of *Gymnema sylvestre* and soya lecithin and phytosome complex of *Gymnema sylvestre* were placed in the aluminium crimp cell and heated at 10ºC/min from 0 to 400ºC in the atmosphere of nitrogen. Peak transition onset temperatures are recorded by means of an analyzer (Zhang et al. 2013).

**SEM Analysis**

Scanning electron microscopy is used to determine particle size distribution and surface morphology of the complexes. Dry samples are placed on an electron microscope brass stub and coated with gold in an ion sputter. Digital images of phytosome complex of *Gymnema sylvestre* were taken by random scanning of the stub at 1000, 5000, 10000 and 30000 X magnifications (Zhi-peng et al. 2010).

***In-vitro* drug release**

The membrane is mounted over a Franz diffusion cell and formulated phytosomes. The receiver compartment of the diffusion cell is filled with 15.0 ml of PBS pH 7.4 and the mixture is kept over a magnetic stirrer and temperature maintained at 37°C. Sample of 3 ml is withdrawn and replenished immediately from the receiver compartment at every 1, 2, 3, 4, 6 and 12h. They are stored in refrigerated condition until the analysis is performed. The content of herbal extracts in the samples is analyzed by UV-Visible spectrophotometer. The concentrations of drug are determined at wavelength 270 nm.

**Stability studies**

Stability studies are carried out by keeping the optimized formulations in the butter paper and covered by aluminum foil and placed in the aluminum pouch. It is sealed by heat at the end for one month at room temperature. The films are taken at different time intervals like 0 to 4th week and are analyzed for its appearance, folding endurance, and drug content.

**Evaluation of anti-diabetic activity *(in-vitro)***

**Estimation of α-amylase**

The alpha-amylase assay is performed according to the method described by Odeyemi [2015]. Briefly, 15$\mu$l of the phytosomes at different concentrations (50$\mu$g/ml – 200$\mu$g/ml) (diluted in a phosphate buffer) was added to 5$\mu$l of enzyme porcine pancreatic solution into 96-well plate. After 10 min of incubation at 37°C, the reaction was initiated by adding 20$\mu$l of starch solution and further incubated for 30 min at 37°C. The reaction is then stopped by adding 10$\mu$l 1M of HCl to each well followed by 75$\mu$l of iodine reagent. A blank containing phosphate buffer (pH 6.9) instead of the phytosome and a positive control (acarbose, 64$\mu$g/ml) is prepared. No enzyme control and no starch control are included for each test sample. The absorbance is measured at 580 nm and the percentage inhibitory activity is calculated by using the following equation:

$$\text{Inhibition (\%)} = 100 - \text{\% reaction (at min)}$$

Where % reaction = mean maltose in sample × 100/mean maltose in control.

**Estimation of α-glucosidase**

To 50µl of phytosomes concentration in a test tube (0-40ug/ml) the following are added sequentially: buffered α-glucosidase (100µL, 1.0U/ ml) and incubated at 37ºC for 10minutes, then pNPG (50µl, 3.0mM) and incubated at 37ºC, for 20 min, then $Na_2CO_3$ (5%w/v), cooled to 25ºC and lastly 5 ml $H_2O$ is added and vortexed (Ononamadu et al. 2019). The absorbance

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of the yellow p-nitrophenol from the different test tubes will be taken at 405nm and the percentage inhibition was calculated as follows;

$$\% \text{ Inhibition} = Ac - At/Ac \times 100$$

## RESULTS AND DISCUSSION

### Pre-formulation study

### Organoleptic properties

The hydro-ethanolic leaves extract of *Gymnema sylvestre* was found as green-brownish powder with its characteristic odor. Soya lecithin was found as brown liquid with its characteristic odor.

**Table 2. Organoleptic properties of *Gymnema sylvestre* and Soya lecithin**

| Plant extract | Organoleptic characteristics | | |
|---|---|---|---|
| | Appearance | Colour | Odor |
| *Gymnema sylvestre* | Powder | Green-brownish | Characteristics |
| Soya lecithin | Liquid | Brown | Characteristics |

### Solubility estimation

In Dichloromethane and n-hexane, *Gymnema sylvestre* extract was found poorly soluble. Moreover, Soya lecithin was found highly soluble in Dichloromethane and n-hexane solvents.

**Table 3. Solubility studies**

| Solvent | *Gymnema sylvestre* | Soya lecithin |
|---|---|---|
| Dichloromethane | Poorly soluble | Highly soluble |
| n-hexane | Poorly soluble | Freely soluble |

### Preparation of Std. Calibration curve of *Gymnema sylvestre*

The following table shows the conc. (µg/ml) of *Gymnema sylvestre* leaves extract and absorption (λmax 220 nm).

**Table 4. Absorption of *Gymnema sylvestre* leaves extract**

| Conc. (µg/ml) | Absorption (λmax 220 nm) |
|---|---|
| 2 | 0.17 |
| 4 | 0.35 |

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| | |
|---|---|
| 6 | 0.54 |
| 8 | 0.79 |
| 10 | 0.95 |

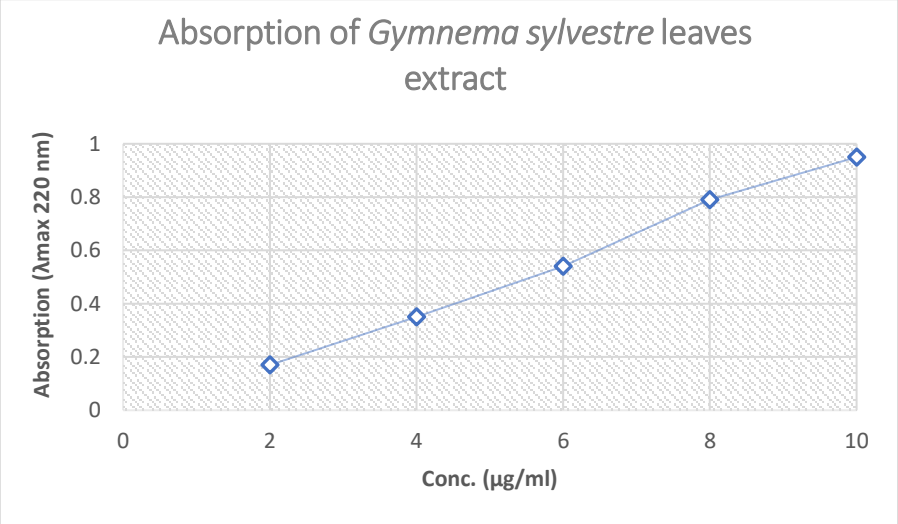


**Fig 2. Std. Calibration Curve of *Gymnema sylvestre* leaves extract**

**Preparation of Std. Calibration curve of Soya lecithin**

The following table shows the conc. (µg/ml) of Soya lecithin and absorption (λmax 260 nm).

**Table 5. Absorption of Soya lecithin**

| Conc. (µg/ml) | Absorption (λmax 260 nm) |
|---|---|
| 2 | 0.14 |
| 4 | 0.33 |
| 6 | 0.52 |
| 8 | 0.78 |
| 10 | 0.93 |

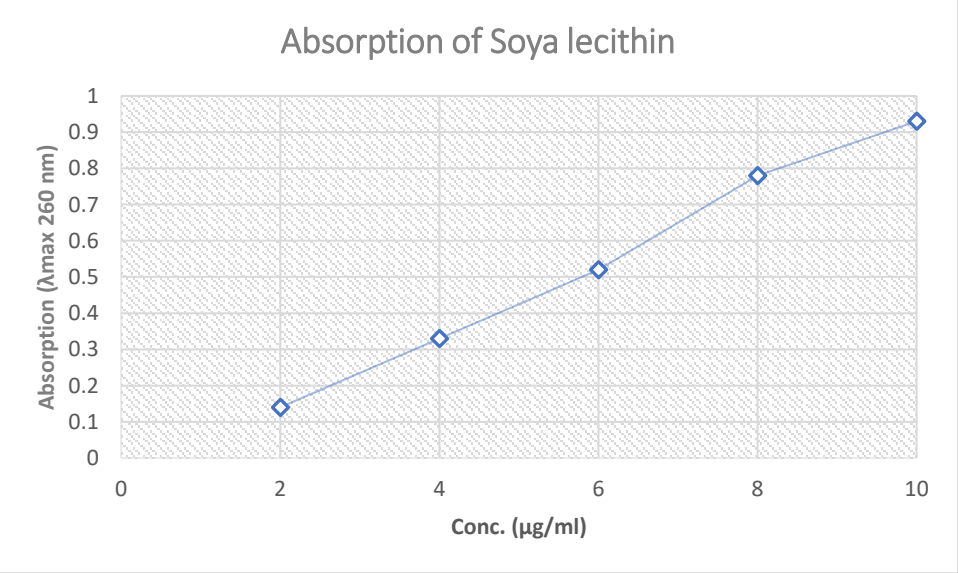

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**Fig 3. Std. Calibration Curve of Soya lecithin**

**Characterization parameters**

**Physical appearance**

Phytosomes were observed as homogenous and brown in color.

**Table 6. Physical appearance of *Gymnema sylvestre* phytosomes**

| Formulation | Physical appearance |
|---|---|
| F1 | Brown; homogenous |
| F2 | Brown; homogenous |
| F3 | Brown; homogenous |
| F4 | Brown; heterogenous |

**Solubility estimation**

**Table 7. Solubility of *Gymnema sylvestre* phytosomes**

| Formulation | Solubility | | | |
|---|---|---|---|---|
| | Ethanol | Methanol | Phosphate Buffer | Water |
| F1 | Soluble | Highly Soluble | Soluble | Soluble |
| F2 | Soluble | Highly Soluble | Soluble | Soluble |
| F3 | Soluble | Highly Soluble | Soluble | Soluble |
| F4 | Soluble | Highly Soluble | Soluble | Soluble |

**Droplet size**

Phytosome's droplet size was estimated using nanodroplet analyser. Droplet size was determined as low in F3 as 21.16±0.21 nm. While it was observed increased in the case of F4, F1 and F2 as 23.45±0.27 nm, 29.31±0.42 nm and 26.34±0.10 nm, respectively.

**Table 8. Droplet size (nm) of *Gymnema sylvestre* phytosomes**

| Formulation | Droplet size (nm) |
|---|---|
| F1 | 29.31±0.42 |
| F2 | 26.34±0.10 |
| F3 | 21.16±0.21 |
| F4 | 23.45±0.27 |

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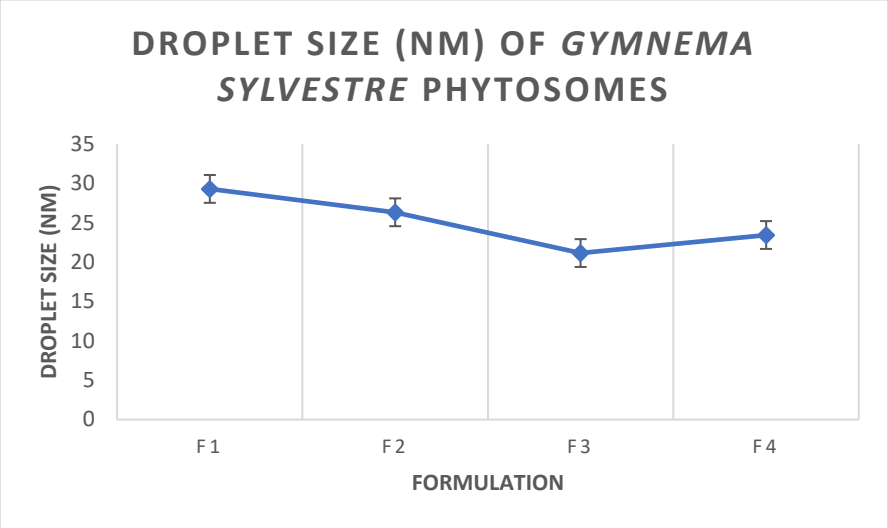


**Fig 4. Droplet size (nm) of *Gymnema sylvestre* phytosomes**

**Determination of Polydispersity Index (PDI)**

Polydispersity index is an important factor in evaluation of topical dosage forms for their uniformity of particles. PDI was observed least in F3 as 0.47±0.18. It might be due to increased proportion of surfactants used during formulation of phytosomes.

Below Table depicts the PDI as below-

**Table 9. Polydispersity Index of *Gymnema sylvestre* phytosomes**

| Formulation | PDI |
|---|---|
| F1 | 0.59±0.17 |
| F2 | 0.53±0.10 |
| F3 | 0.47±0.18 |
| F4 | 0.51±0.14 |

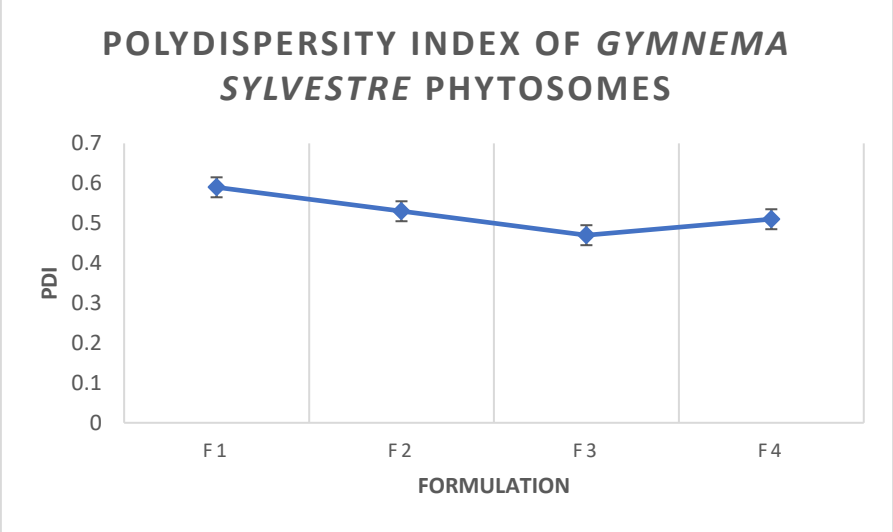

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**Fig 5. Polydispersity Index of *Gymnema sylvestre* phytosomes**

**Entrapment efficiency**

Entrapment efficiency was noted as 83.27±0.19 %, 81.16±0.34 %, 89.10±0.21 % and 86.52±0.13 % in F1, F2, F3 and F4, respectively.

Below Table demonstrates the entrapment efficiency-

**Table 10. Entrapment efficiency of *Gymnema sylvestre* phytosomes**

| Formulation | Entrapment efficiency (%) |
|---|---|
| F1 | 83.27±0.19 |
| F2 | 81.16±0.34 |
| F3 | 89.10±0.21 |
| F4 | 86.52±0.13 |

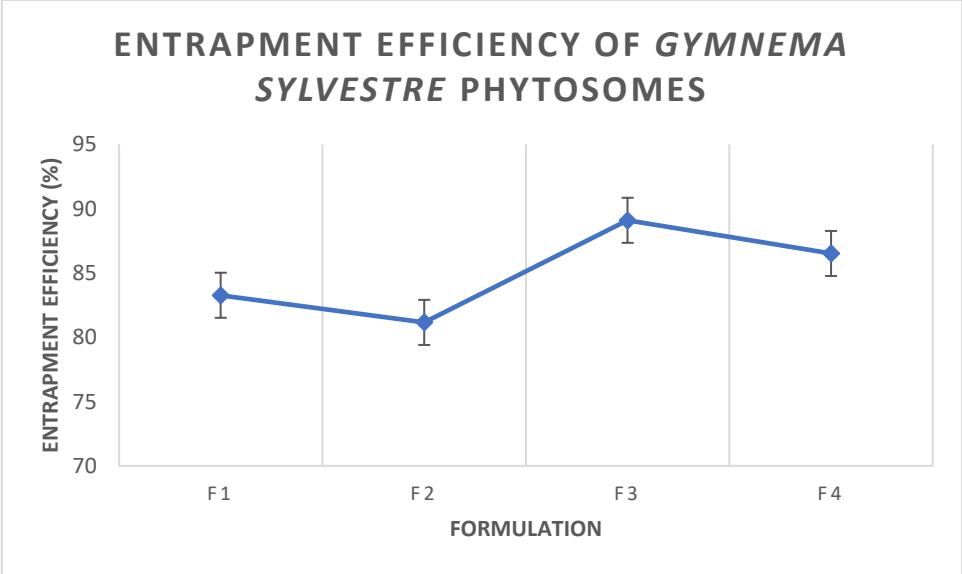
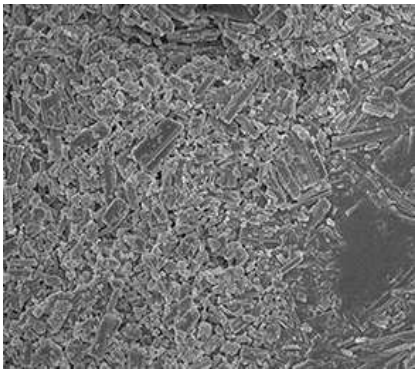


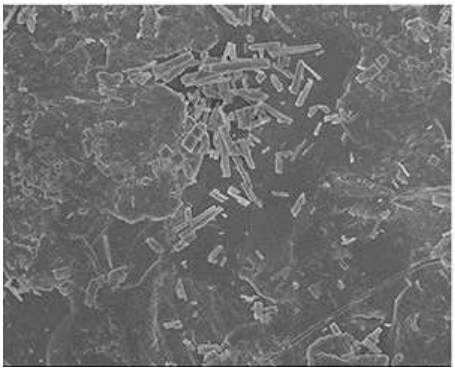

**Fig 6. Entrapment efficiency of *Gymnema sylvestre* phytosomes**

**SEM Analysis**

SEM analysis of phytosomes was observed as followings:



**F1**



**F2**

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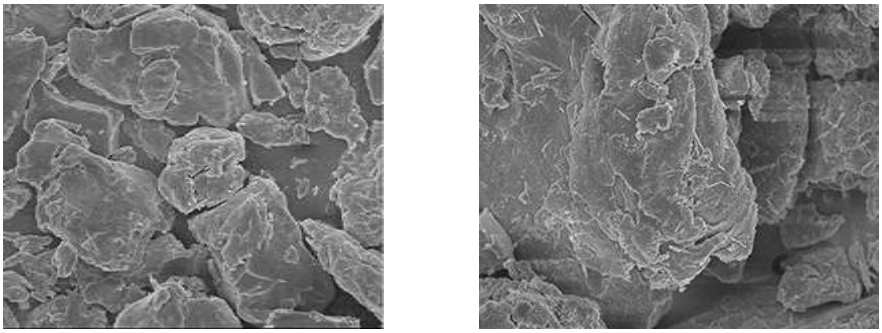

F3 F4

**Fig. 7. SEM Analysis of *Gymnema sylvestre* phytosomes**

***In-vitro* drug release**

It was found excellent when compared that all phytosomes showed better drug release. After 12 hour, *in-vitro* drug release was estimated as 93.17±0.4, 94.24±0.4, 95.39±0.1 and 94.26±0.2 in F1, F2, F3 and F4.

**Table 11. *In-vitro* drug release of *Gymnema sylvestre* phytosomes**

| Time (hr) | *In vitro* drug release | | | |
|---|---|---|---|---|
| | F1 | F2 | F3 | F4 |
| 0 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1 | 7.82±0.2 | 9.10±0.6 | 10.29±0.4 | 9.31±0.4 |
| 2 | 12.29±0.1 | 16.43±0.2 | 14.11±0.2 | 13.25±0.3 |
| 4 | 16.40±0.2 | 17.11±0.3 | 18.29±0.1 | 17.20±0.1 |
| 6 | 27.14±0.2 | 30.16±0.2 | 31.10±0.6 | 29.45±0.6 |
| 8 | 52.31±0.6 | 54.34±0.3 | 57.16±0.4 | 56.18±0.2 |
| 10 | 71.24±0.2 | 73.10±0.2 | 75.23±0.2 | 72.19±0.4 |
| 12 | 93.17±0.4 | 94.24±0.4 | 95.39±0.1 | 94.26±0.2 |

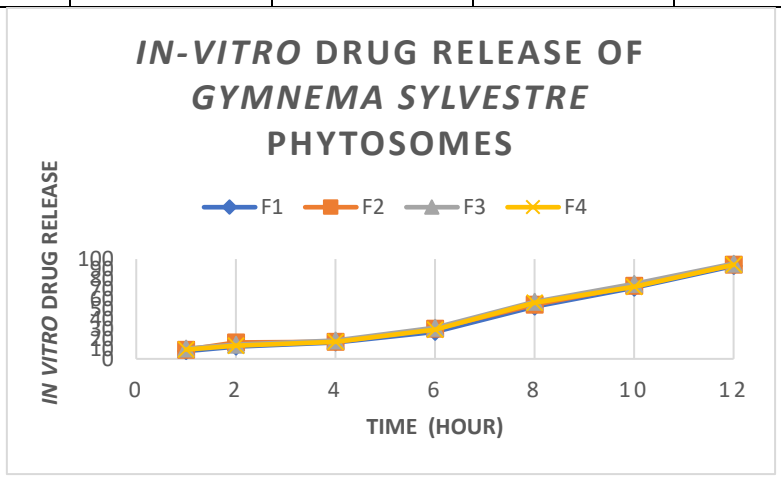

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**Fig 8. *In-vitro* drug release of *Gymnema sylvestre* phytosomes**

**Stability Studies**

Stability studies are carried out by keeping the phytosomes in the butter paper and covered by aluminum foil and placed in the aluminum pouch. It was sealed by heat at the end for one month at room temperature. The phytosomes were taken at different time intervals like 0 to 4th weeks and were found in its original appearance. Moreover, the folding endurance was found almost similar as previous.

**Evaluation of anti-diabetic activity *(in-vitro)***

**Estimation of α-amylase**

In α-Amylase inhibition (% Inhibition), water, Phytosome (F3) and acarbose were estimated for different concentrations i.e., 200µg/ml, 400µg/ml and 800µg/ml. The % inhibition of Phytosome (F3) was compared with acarbose.

The α-Amylase inhibition is an important feature for estimation of anti-diabetic potential. At 800µg/ml, the α-Amylase inhibition was estimated as 72.23±0.07 %, and 94.45±0.11 %, in Phytosome (F3) and acarbose, respectively.

Therefore, it can be easily observed that Phytosome (F3) showed an effective α-Amylase inhibition when compared with control

**Table 12. Estimation of α-amylase inhibition of Phytosome (F3)**

| Concentration (µg/ml) | α-Amylase inhibition (% Inhibition) | | |
|---|---|---|---|
| | Water | Phytosome (F3) | Acarbose |
| 200µg/ml | 21.39±0.29 | 34.28±0.19 | 59.10±0.27 |
| 400µg/ml | 33.14±0.25 | 43.19±0.32 | 71.24±0.15 |
| 800µg/ml | 45.26±0.37 | 72.23±0.07 | 94.45±0.11 |

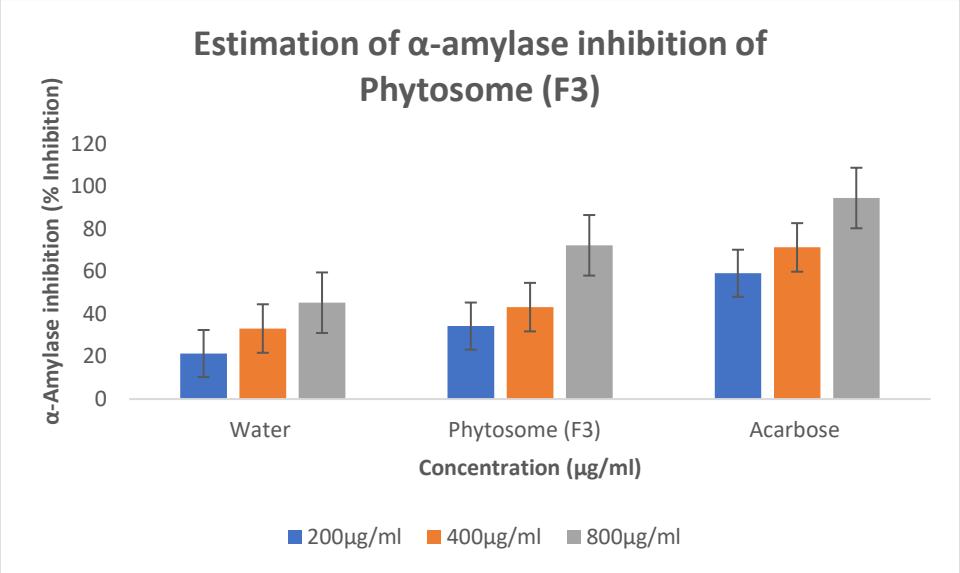


**Fig 9. Estimation of α-amylase inhibition of Phytosome (F3)**

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**Estimation of α-glucosidase**

In α-glucosidase inhibition (% Inhibition), water, Phytosome (F3) and acarbose were estimated for different concentrations i.e., 200µg/ml, 400µg/ml and 800µg/ml. The % inhibition of Phytosome (F3) was compared with acarbose.

As compared with α-Amylase inhibition, it showed much prominent % inhibition of α-glucosidase. The acarbose was used as a reference. The α-glucosidase inhibition in Phytosome (F3) was observed as 34.10±0.45 %, 47.29±0.05 % and 68.36±0.19 % in the concentration of 200µg/ml, 400µg/ml, 800µg/ml, respectively.

The antidiabetic potential was observed in ascending order as response increased as the dose increases.

**Table 13. α-glucosidase inhibition of Phytosome (F3)**

| Concentration (µg/ml) | α-Glucosidase inhibition (% Inhibition) | | |
|---|---|---|---|
| | Water | Phytosome (F3) | Acarbose |
| 200µg/ml | 24.45±0.10 | 34.10±0.45 | 58.15±0.27 |
| 400µg/ml | 22.14±0.20 | 47.29±0.05 | 72.45±0.16 |
| 800µg/ml | 25.10±0.54 | 68.36±0.19 | 96.15±0.39 |

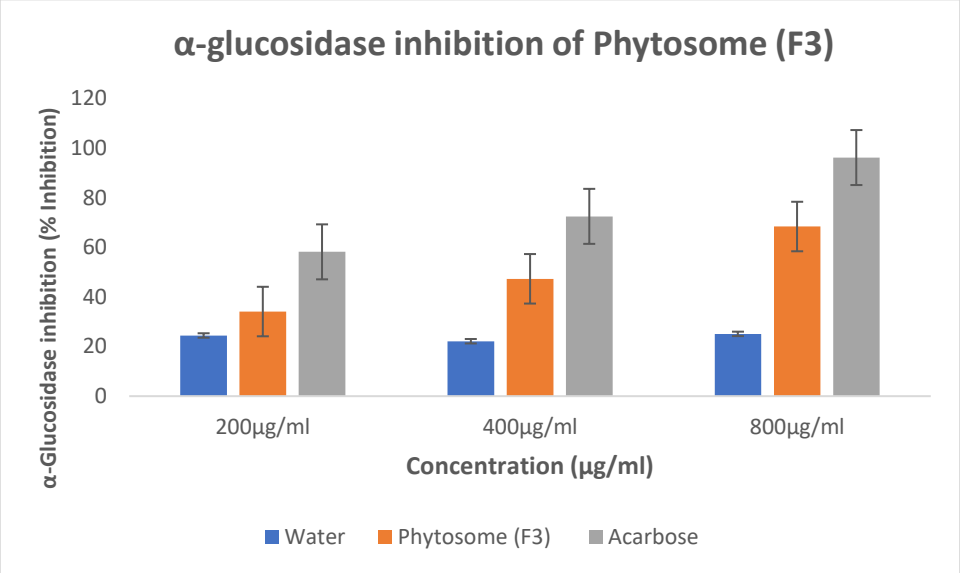


**Fig 10. Estimation of α-glucosidase inhibition of Phytosome (F3)**

The restoration of damaged beta-cells and safeguard beta cells from oxidative stress in diabetic rats during experimental trials. A study has found that Artemisia afra has hypoglycemic effect in diabetic rabbits. This activity is attributed to the presence of Saponins, which may stimulate the production of insulin via repairing pancreatic beta cells. Additionally, some of the bioactive components in this study may enhance the activity of glycolytic and glyconeogenic enzymes either synergistically or independently (Wolde et al. 2016).

A commonly recognized fact is that the decrease in postprandial hyperglycemia can be accomplished by impeding the action of intestinal α-glucosidase and pancreatic α-amylase,

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which leads to a delay in carbohydrate digestion (Aloulou et al. (2012). The plant's crude extract and solvent fractions exhibited inhibitory effect against pancreatic α-amylase. The exploration for novel medicines derived from natural resources, particularly medicinal plants, is an appealing strategy for addressing postprandial hyperglycemia. The ethyl acetate solvent fraction exhibited the highest level of inhibition (54.23%), whereas the aqueous fraction demonstrated the lowest level of effectiveness (26.18%). The ethyl acetate extract is highly likely to contain semi-polar compounds that exhibit α amylase inhibiting activity. It is advisable to do further investigation and isolate the pure active compounds. Flavonoids, etc. are prominent polyphenolic chemicals known for their ability to block α-amylase. The phytochemical examination of the extracts indicated a high concentration of polyphenolic compounds, indicating that the bioactive substance responsible for inhibiting α-amylase may be present in all plant extracts, albeit at varying amounts. The crude extract exhibited the highest level of anti-oxidant activity at 58.38%, whereas the aqueous fraction showed the lowest level of antioxidant activity at 36.52%. An intriguing aspect of our investigation was that the crude extract exhibited superior antioxidant capacity compared to the solvent fractions. The *H. abyssinica* extract exhibited antioxidant activity that was depending on the dosage. The floral crude extract, DW10, did not have a significant impact on the blood glucose levels of fasted normoglycemic mice in terms of its hypoglycemic action. It was discovered that the extract's effect was dependent on the dosage. The crude extract exhibited a delayed although notable reduction in blood sugar levels, indicating that the extract's ability to lower blood sugar increased over time. The maximum effect was observed at the 6th hour (Kim et al. 2000). The plant extract exhibited a relatively delayed beginning of hypoglycemic activity compared to the usual medication. The hypoglycemic impact of glibenclamide is evident since it stimulates insulin release from pancreatic β-cells and inhibits glucagon secretion. It may possess an insulinomimetic action or elicit insulin production from β-cells (Kim et al. 2000).

## CONCLUSION

It concludes that *Gymnema sylvestre* phytosomes (F3) was most prominent phytosomes among all the phytosome subtypes. It also demonstrated a better stability that can be kept for a month without change in its physical appearance, entrapment and *in-vitro* drug release. Development of *Gymnema sylvestre* phytosomes (F3) might be very significant in terms of managing diabetes mellitus and associated symptoms as well.

This formulation could be confirmed by the *in-vivo* evaluation, after it can be employed for the treatment and diabetes mellitus in human individuals. It can counter the insulin de-sensitivity by facilitating the insulin sensitivity to its binding receptors (Tyrosine kinase).

## CONFLICT OF INTEREST

Authors declare for none conflict of interest.

## FUNDING

Nil.

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