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Evaluation of anti-diabetic activity of *Syzygium cumini* extract and its phytosome formulation against streptozotocin-induced diabetic rats

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Abstract
The Inner kernel of *Syzygium cumini* seeds were extracted and formulated in to a novel phytosome formulation by using cholesterol and lecithin with suitable method. The prepared *Syzygium cumini* seed extract and *Syzygium cumini* phytosome were studied for the acute oral toxicity, Oral glucose tolerance test (OGTT) and anti-diabetic activity against Streptozotocin-induced rats model. The OGTT and antidiabetic activity was compared with control group (1% w/v gum acacia); the standard drug Glibenclamide (50 mg/kg/po), *Syzygium cumini* seed extract (100 / 200 and 400mg/kg/po) and its *Syzygium cumini* phytosome formulation (100 / 200 and 400mg/kg/po). Acute toxicity studies show no mortality and morbidity up to the dose 2000mg/kg of body weight. In OGTT, and antidiabetic activity studies *Syzygium cumini* seed extract and *Syzygium cumini* phytosome formulation shows a significant control in blood sugar level in comparison with standard drug Glibenclamide in a dose dependent manner. Further the research proves that phytosome formulation is superior in controlling blood sugar than *Syzygium cumini* seed extract.

Keywords: OGTT, Anti diabetic, *Syzygium cumini* Phytosome complex, cholesterol and lecithin

Introduction
Plant components or their extracts are widely employed in the preparation of medicines since past and nowadays the use of Phyto medicines for therapeutic purposes is fast emerging. Phyto constituents have a drawback that they are restricted in their effectiveness due to their poor absorption and restricted solubility in water. Further phyto constituents cannot simply get absorbed and their passage through the lipoidal biological membrane is forbidden due to its double-layered surface of all cells and high polarity and poor lipophilicity [1]. Several approaches are developed to enhance the bioavailability of the phyto constituents, like the inclusion of solubility and bioavailability enhancers, structural modification and inclusion of the lipotropic carriers. Phospholipids play much important role in the development of novel phytopharmaceuticals due to its biocompatible nature with the phytochemicals.

Many studies have urged the useful role of phospholipids in enhancing the therapeutic efficiency of phytochemicals having poor oral absorption. Therefore, a unique approach is important to extend the bioavailability of such compounds for higher clinical utility. Phyto somes area is a unit of novel drug phyto formulations containing active phyto constituents encapsulated lipid molecule layer. Phyto somes shows higher absorption since the water soluble constituent is coated by a lipotropic outer layer and thus show higher bioavailability than the traditional herbal extracts.

The term "Phyto" means plant and "some" means cell like. The phytosome method has conjointly been applied to several types of herbal extracts such as *Ginkgo biloba, grape seed, hawthorn, milk weed, green tea, and ginseng*. The flavonoid and terpenoid elements of those flavoring extracts lend themselves quite well for the direct binding to phosphatidylcholine [2].

Diabetes mellitus is a general disorder characterized by increase in glucose level as a result of insufficient secretion of insulin hormone and lack of its action. It conjointly involves DKA (ketoacidosis) and ketones, kidney disease (nephropathy), eye complications, gastroparesis, heart disease, high blood pressure (hypertension), hyperosmolar hyperglycemic nonketotic syndrome (HHNS), mental health, neuropathy foot complications, pregnancy related conditions, skin complications and stroke diseases [3].

Managing polygenic disease of *Diabetes mellitus* with presently accessible medication has unwanted harmful effects and a challenging one. Thus, the research still continues for newer diabetic agent. The rising technology of drug delivery and drug targeting is being applied to phytopharmaceuticals in recent time and the foremost factors for drug molecules to penetrate the biological membranes to be absorbed consistently irrespective of their lipid solubility molecular size.

The phytosome technology produces a little micro sphere or little cell, which protects the plant extract or its active constituent from destruction by gastric secretion and gut bacteria due to the gastro protective property of phosphatidylcholine. This phyto-phospholipid complex resembles a little cell which exhibit better pharmacokinetic and pharmacy dynamic profile than the conventional herbal extract resulting in better bioavailability [4].

Syzygium cumini (Linn.) Skeels also known as *Eugenia jambolana* belongs to family My rtaceae, a well-known tree of Indian subcontinent and adjoining regions of Southeast Asia, Australia, across India, Bangladesh, Pakistan, Nepal, Sri Lanka, Malaysia, the Philippines, and Indonesia. It is grown in a variety of habitats, river banks, scrub are planted as avenue trees, up to a height of 1400m. Fruit is a berry and appears in clusters of just a few or 10-40, are round or oblong, often curved, 1.25-5 cm long, turning from green to light-magenta, then dark-purple or nearly black. The skin was found to be thin, smooth, glossy, and adherent. The pulp is purple or white, very juicy, and normally encloses a single, oblong, green or brown seed, up to 4 cm long. The fruit is usually astringent, and the flavor varies from acid to fairly sweet.

Seeds of *Syzygium cumini* contains, a trace of pale yellow essential oil, fat, resin, albumin, chlorophyll, an alkaloid-jambosine, gallic acid, ellagic acid, corilagin and related tannin,3,6-hexahydroxy diphenoyl glucose and its isomer 4,6-hexahydroxydi phenoyl glucose, 1-galloylglucose, 3-galloylglucose, quercetin and elements such as zinc, chromium, vanadium, potassium and sodium. Unsaponifiable matter of seed fat contains β-sitoterol. The presence of gallic acid, ellagic acid and related ellagi - tannins, other tannins and polyphenols was confirmed. It was found that various extracts of fruit and seeds of *Syzygium cumini* had anti-diabetic, anti-inflammatory, hepatoprotective, antihyperlipidemic, diuretic and antibacterial activities. These properties of *Syzygium cumini* seeds are due to the presence of phenols, saponins, tannins and flavonoids [5, 6, 7].

Preparation of seed extract

The seeds of the *Syzygium cumini* were processed by the removal of the fruits outer coating and the inner kernel alone were taken, dried under shade, powdered by using seed crushing machine and sieved under 40 mesh. The preparation of hydro alcoholic extracts were carried out in the ratio 70:30 % v/v (alcohol: water) by using Soxhlet's apparatus for 48 hrs. The freeze dried hydro ethanolic *Syzygium cumini* extract was used for further studies.

Preparation of *Syzygium cumini* phytosomes complex

The aqueous extract of *Syzygium cumini* (10mg) was dissolved in 20 ml of distilled water and hydrated with dried layers of cholesterol (15 mg) and lecithin (40 to 60mg) in the round bottom flask and the mixture was rotated in a water bath at 40 ± 2ºC for 1 hr. The complex was then sonicated using 3 mm spindle ultra sonicator (Vibronics). The phytosome vesicles containing *Syzygium cumini* extract which were formed, was subsequently further subjected to ultra-sonication for 10 to 20min to get spherical vesicles. The formed Phytosome suspension was freeze dried to obtain dry powder by using freeze drier (Lark, Haryana, India).The prepared phyto somes were stored in refrigerator (10 to 20◦ C) for further evaluations.

Acute oral toxicity

Acute oral toxicity was performed as per Organization for Economic Co-operation and Development (OECD) 423 guidelines. The institutional ethical committee of RVS College of Pharmacy, Coimbatore, Tamil Nadu, India has approved the protocol for these experiments. (RVSCOPS/IAEC/2018/003dated 10.02.2018). The experiments were performed using healthy young female Wistar rats, nulliparous of 160-180g. Feminine rats were chosen owing to their higher sensitivity to treatment and they were acclimatized to standard laboratory conditions for seven days. Animals were fed normal rat diet *ad libitum* and were allowed free access to water. The rats were housed in polypropylene confines (55 x 32.7 x 19 cm), with sawdust litter in a temperature controlled condition (23 ± 2ºC). Lighting was controlled to supply 12 h of light and 12 h of dim light for every 24-h period. Each gauge was recognized by a card which expressed the rat's number, weight of the creatures it contained, test substance code, organization of groups and measurement level [8].

Mode of test substance administration

The test substance was controlled in a solitary dosage by gavages utilizing extra ordinarily planned rat oral needle. Rats were fasted 3 h preceding dosing (just pallet diet was withheld for 3 h, however not water). Following the time of fasting, rats were weighed and test substance was administered orally at a measurement of 5, 50,300 and 2000 mg/kg. After the administration of test substance, pallet diet for the rats was withheld for 2 h. The administration volume was 1ml/kg body weight of the rat's equivalent to the dose specified in the groups was given by considering the body weight of the rats upon the arrival of treatment, the amount of the test substance was computed.

Observation period

Rats were observed after an initial period of 30 min, then periodically for the next 24 h, with unique consideration being given for the first initial 3 h, and then, day by day from that point, for a period of 14 days. The rats were observed at least twice daily with the purpose of recording any symptoms of sick / well-being or behavioral changes.

Signs recorded during acute toxicity studies

The observation parameters include coma, convulsions, diarrhea, lethargy, salivation, sleep and tremors. Autonomic and central nervous systems behavior pattern, circulatory, eyes and mucous membrane, respiratory, skin and fur and somatomotor activity are the other parameters observed. The time of death, if any, was also recorded. After administration of the test substance, food was withheld for a further period of 1-2 h. The number of survivors was noted after 24 h and then these were maintained for a further period of 14 days with daily observation.

Statistical Analysis
Data are presented as a mean ± SEM (Standard Error of the Mean). Comparisons were made between the treated groups of animals by the use of single way Analysis of Variance (ANOVA) followed by Dunnett's test. All data were analyzed using SIGMA STAT version 3.1. $P< 0.05$ which was considered as the level of statistical significance.

Oral Glucose Tolerance Test of *Syzygium cumini* Extract
Male Wistar rats (140 ± 20 g) were chosen and kept for an overnight starvation. Next morning, the blood glucose level (0 min) of every rat was estimated by glucometer utilizing accucheck glucose trips. The rats demonstrating their fasting blood glucose levels in the range of 60-80 mg/dL were chosen and isolated into one control group (Group –I) and five experimental groups (Group –II to V) with six animals in each group. The test drugs were given just half an hour before administration of glucose. Each rat was administered with a fine suspension of the test substances prepared in 1.0%w/v gum acacia. Group –I was given only 1.0%w/v gum acacia while Group –II was administered with Glibenclamide (5mg/kg) as Standard, Group –III with 100mg/kg of the test drug; Group –IV with 200mg/kg of the test drug and Group –V with *Syzygium cumini* extract 400mg /kg. Precisely 30 min post-organization of the tests/vehicle, an oral glucose of 10 g/kg bw was given to rats and the blood glucose levels were estimated at 0 min, 30 min, 1st hour, 2nd and 3rd hour after the treatment [9].

Anti-diabetic activity of *Syzygium cumini* extract against Streptozotocin-induced rats
Streptozotocin (STZ) -induced diabetic male albino Wistar rats (150 ± 20 g) were chosen for this examination. Diabetes was initiated in the rats by intraperitoneally infusing freshly prepared STZ in 0.1M citrate (pH 4.5) at a dose of 60 mg/kg body weight. The blood glucose of every rat was checked after 72h and rats demonstrating fasting blood glucose esteems between 280-450 mg/dL were chosen. A steady state is reached after 10 days and the rats were allowed for diabetic tests. These diabetic rats were randomly divided into groups consisting of six animals in each. Control Group –I received vehicle (1% w/v gum acacia) and the animals of the experimental groups were orally given in the form of fine suspension in 1% w/v gum acacia. Group –II Diabetic control; Group –III standard Glibenclamide (5mg/kg); Group –IV *Syzygium cumini extract* 100mg/kg; Group –V *Syzygium cumini extract* 200mg /kg and Group –VI *Syzygium cumini* extract 400mg /kg. Blood tests were performed by tail nipping and blood glucose level was checked by Accucheck at initial, 7th day, 14th day, 21stday and 28th day individually [10].

Oral Glucose Tolerance Test of *Syzygium cumini* Phytosome Formulation
Male Wistar rats (140 ± 20 g) were chosen and kept for an overnight starvation. Next morning, the blood glucose level (0 min) of every rat was estimated by glucometer utilizing accucheck glucostrips. The rats demonstrating their fasting blood glucose levels in the range of 60-80 mg/dL were chosen and isolated into one control group (Group –I) and four experimental groups (Group –II to V) with six animals in each group. The test drugs were given just half an hour before administration of glucose. Each rat was administered with a fine suspension of the test substances prepared in 1.0%w/v gum acacia. Group –I was given only 1.0%w/v gum acacia while Group –II was administered with Glibenclamide (5mg/kg) as Standard, Group –III with 100mg/kg of *Syzygium cumini* phytosome formulation; Group –IV with 200mg/kg of *Syzygium cumini* phytosome formulation and Group –V with of *Syzygium cumini* phytosome formulation 400mg /kg. Precisely 30 min post-organization of the tests/vehicle, an oral glucose of 10 g/kg bw was given to rats and the blood glucose levels were estimated at 0 min, 30 min, 1st hour, 2nd and 3rd hour after the treatment [9].

Anti-diabetic activity of *Syzygium cumini* phytosome formulation against Streptozotocin-induced rats
Streptozotocin (STZ) -induced diabetic male albino Wistar rats (150 ± 20 g) were chosen for this examination. Diabetes was initiated in the rats by intraperitoneally infusing freshly prepared STZ in 0.1M citrate (pH 4.5) at a dose of 60 mg/kg body weight. The blood glucose of each rat was checked after 72h and rats demonstrating fasting blood glucose esteems between 280-450 mg/dL were chosen for the study. A steady state is reached after 10 days and the rats were allowed for diabetic tests. These diabetic rats were randomly divided into groups consisting of six animals in each. Control Group –I received vehicle (1% w/v gum acacia) and the animals of the experimental groups were orally given in the form of fine suspension in 1% w/v gum acacia. Group –II Diabetic control; Group –III standard Glibenclamide (5mg/kg); Group –IV *Syzygium cumini* phytosome formulation 100mg/kg; Group –V *Syzygium cumini* phytosome formulation 200mg /kg and Group –VI *Syzygium cumini* phytosome formulation 400mg /kg. Blood tests were performed by tail nipping and blood glucose level was checked by Accucheck at initial, 7th day, 14th day, 21stday and 28th day individually [10].

Table 1: Results of acute toxicity studies of *Syzygium cumini* extract

Group	Dose (mg/kg)	No. of animals	Dose Difference (a)	Animals died (b)	Mean	Product (a x b)
1.	5	6	0	–	–	–
2.	50	6	45	–	–	–
3.	300	6	250	–	–	–
4.	2000	6	1750	–	–	–

LD_{50} = higher dose – Σ (a x b)/ n where n = No. of animals in each group
LD_{50} = 2000– 0 = 2000 mg / kg; ED_{50} = LD50 / 10 = 2000 / 10 = 200mg / kg

Table 2: Results of acute toxicity studies in rats treated with *Syzygium cumini* extract.

Observation	**Effect**								
Gross behaviour activity	Up to 3hrs	3 ½ hrs	4 hrs	4 ½ hrs	5 hrs	5 ½ hrs	6 hrs	12 hrs	24 hrs
Respiration	N	N	N	N	N	N	N	N	N
Writhing	-	-	-	-	-	-	-	-	-
Tremor	-	-	-	-	-	-	-	-	-
Convulsions	-	-	-	-	-	-	-	-	-
Hind limb paralysis	-	-	-	-	-	-	-	-	-
Sense of touch and sound	N	N	N	N	N	N	N	N	N
Salivation	N	N	N	N	N	N	N	N	N
Urination	+	+	+	+	+	+	+	+	+
Diarrhoea	-	-	-	-	-	-	-	-	-
Mortality	-	-	-	-	-	-	-	-	-

(-) No Effect **(N)** Normal effect

Table 3: Results of oral glucose tolerance test - *Syzygium cumini* extract

Group	**Blood glucose levels (mg/dl)**				
	0 min	30 min	1st hour	2nd hour	3rd hour
Group –I (Control)	73.5 ± 1.15	120.4 ± 1.41	161.81 ± 11.60	140.15± 2.64	110.13 ± 5.75
Group –II [Standard Glibenclamide (5mg/kg)	76.5 ± 10.16	70.1 ± 7.02**	89.0 ± 10.61**	86.6 ± 12.32**	82.5 ± 7.80**
Group –III (*Syzygium cumini* extract 100mg/kg)	72.2±1.23	111.8±2.04*	142.23±5.06*	131.11±8.61*	100.42±4.27*
Group –IV (*Syzygium cumini* extract 200mg/kg)	75.7 ± 5.26	82.6 ± 5.893**	82.9 ±1.93**	90.1±2.41**	80.5 ± 1.52**
Group –V (*Syzygium cumini* extract 400mg /kg)	78.5±1.22	81.5±0.22**	79.05±1.22**	79.3±2.5**	79.5±2.5**

Values are mean ± SEM; n=6 in each group; Group –II to Group V was compared with Group-I the values of Oral glucose tolerance test were altered significantly (**= P<0.01) moderately significant, (*= P<0.05 significant).

Table 4: Results of oral glucose tolerance test - *Syzygium cumini* phytosome formulation

Group	Blood glucose levels (mg/dl)				
	0 min	30 min	1st hour	2nd hour	3rd hour
Group –I (Control)	73.5 ± 1.15	120.4 ± 1.41	161.81 ± 11.60	140± 2.64	110.13 ± 5.75
Group –II [Standard Glibenclamide (5mg/kg)]	76.5 ± 10.163	70.1 ± 7.2**	89.0 ± 10.61***	86.6 ± 12.32***	82.5 ± 7.80**
Group –III (*Syzygium cumini* phytosome formulation 100mg/kg)	72.4±1.45	114.5±2.6	141.56±4.9*	111.15±9.06*	126.54±4.8*
Group –IV (*Syzygium cumini* phytosome formulation 200mg/kg)	76.25 ± 5.245	83.5 ± 5.456**	83.54 ± 2.53***	92.0± 1.91**	81.12 ± 1.92**
Group –V (*Syzygium cumini* phytosome formulation 400mg /kg)	77.48±1.32	80.5±0.25**	80.15±1.12***	80.83±2.69**	80.9±1.99**

Values are mean ± SEM; n=6 in each group; Group –II to Group V was compared with Group -I the values of Oral Glucose Tolerance Test were altered significantly. *** = P<0.001 highly significant; **= P<0.01 moderately significant, *= P<0.05 significant.

Table 5: Results of *Syzygium cumini* extract on blood glucose level in normal control and STZ induced diabetic rats

S. NO	**TREATMENT**	Blood glucose levels (mg/dl)				
		Initial	**7th day**	**14th day**	**21stday**	**28th day**
1.	Group –I (Normal control)	90.17±1.47	95.94±1.30	104.3±4.1	102±2.13	89.52±2.16
2	Group –II (Diabetic control)	263.32±1.44**	262.4±3.62**	300.2±5.4**	373.3±1.7**	404.9±1.63**
3.	Group –III (Diabetic + Glibenclamide (5mg/kg)	258.11±1.3	168.7±3.45a a	150.1±1.4aaa	145.8±0.6aaa	129.6±1.13aaa
4.	Group –IV (Diabetic+ *Syzygium cumini* extract100mg/kg)	267.13±1.5	200.0±2.85 a	208.5±2.3aa	218.78±1.4aaa	224.3±2.57aaa
5.	Group –V (Diabetic+ *Syzygium cumini* extract 200mg/kg)	297.8±1.25	220.5±1.23 a	180.1±0.7aaa	170.2±1.8aaa	130.3±2.79aaa
6	Group –VI (Diabetic+ *Syzygium cumini e*xtract 400mg/kg)	293.9±5.8	182.8±1.15aa	111.3±1.5aaa	89.2±1.4aaa	84.6±3.92aaa

Values are mean ± SEM; n=6 in each group; Group –III to Group VI was compared with Group -II and group- II was compared with group -I the values of blood glucose level were altered significantly.***/ aaa = P<0.001 highly significant; **/ a aa = P<0.01 moderately significant; */aa a = P<0.05 significant.

Table 6: Results of anti-diabetic activity of *Syzygium cumini* phytosome formulation in normal control and STZ induced diabetic rats

S. NO	**TREATMENT**	Blood glucose levels (mg/dl)				
		Initial	**7th day**	**14th day**	**21stday**	**28th day**
1.	Group –I (Normal control)	90.17±1.47	95.94±1.30	104.3±4.1	102±2.13	89.52±2.16
2	Group –II (Diabetic control)	263.32±1.44aaa	282.4±3.62aaa	300.2±5.4aaa	373.3±1.7aaa	404.9±1.63aaa
3.	Group –III (Diabetic + Glibenclamide (5mg/kg)	258.11±1.3	218.7±3.45*	150.1±1.4***	135.8±0.6***	129.6±1.13***
4.	Group –IV (Diabetic + *Syzygium cumini phytosome formulation* 100mg/kg)	267.13±1.5	208.0±2.15*	172.4±2.1**	99.47±1.3***	91.8±2.90***
5.	Group –V (Diabetic+ *Syzygium cumini phytosome formulation* 200mg/kg)	297.8±1.25	200.7±1.11*	139.54±0.59***	91.65±1.9***	86.54±2.83***
6	Group –VI (Diabetic+ *Syzygium cumini phytosome formulation* 400mg/kg)	293.9±5.8	160.65±1.96**	99.3±1.96***	82.34±1.86***	81.12±4.85***

Values are mean ± SEM; n=6 in each group; Group –III to Group VI was compared with Group -II and group- II was compared with group -I the values of blood glucose level were altered significantly.***/ aaa = P<0.001 highly significant; **/ a aa = P<0.01 moderately significant; */aa a = P<0.05 significant.

Results and discussion

Acute toxicity studies

Acute toxicity studies on the rats show no morality at a dose of 2000mg/kg, during a time period of 14 days. During the study, no noticeable events were seen in the rats. This help to predict that it does not contain any type of toxicity and it is full safe. So, 200 mg/kg b.w ($1/10^{th}$ and 500mg/kg b.w ($1/4^{th}$) and 1000mg/kg ($1/2^{th}$) were selected of that dose for the further study. Acute toxicity studies in rats treated with *Syzygium cumini* extract it was observed that at a dose of 2000mg/kg of body weight, there was no mortality. From the acute toxicity studies (as per OECD- 423 guidelines) gross behavior studies in rats the LD_{50} value was determined as 2000mg/kg/oral individually. At this dose levels, no sign of writhing, tremor, convulsion or hind limb paralysis was observed in the mice. Skin, fur, eyes, mucous membrane and behavior pattern were normal. There was no mortality up to the dose level 2000mg/kg and the animals were alive up to the end of the study.

Oral glucose tolerance test-*Syzygium cumini* extract and phytosome formulation

The *Syzygium cumini* extract at a dose of 100, 200 and 400mg/kg significantly reduced the blood glucose level at 30 min after glucose administration in a dose dependent manner. Standard drug Glibenclamide produced activity at all the time interval tested. The Group –II to Group V was compared with Group-I, the values of Oral glucose tolerance test were altered at $P< 0.05$ was considered as the level statistical significance. In a similar way the phytosome formulation reduced Oral glucose tolerance test results in a high statistical significance manner when compared to Group –II to Group V and compared with Group-I. The results proves that the phytosome formulation reduced Oral glucose tolerance test in rats due to fast penetration in lipoidal biological membrane when compared with *Syzygium cumini extract as such the* phyto constituents cannot simply get absorbed and their passage through the lipoidal biological membrane, due to its double-layered surface of all cells and high polarity and poor lipophilicity. The kwon component of cholesterol and lecithin Phytosome formulation has an affinity for fast penetration in lipoidal bilayer.

Blood glucose level in normal control and STZ induced diabetic rats of *Syzygium cumini* extract and phytosome formulation

The *Syzygium cumini* extract at a dose of 100, 200 and 400mg/kg significantly reduced the blood glucose level at on 7^{th},14^{th}, 21^{st} and 28^{th} in STZ induced diabetic rats in a dose dependent manner. Standard drug Glibenclamide produced activity at all the time interval tested. The Group –II to Group V was compared with Group-I, the values of STZ induced diabetic rats were altered at $P< 0.05$; 0.01 and 0.001 was considered as the level statistical significance. In a similar way the phytosome formulation reduced blood glucose against STZ induced diabetic rats in a high statistical significance manner when compared to Group –II to Group V and compared with Group-I.

Discussion

The result proves that the phytosome formulation has a better and fast reduction of glucose in Oral glucose tolerance test and STZ induced diabetic rats. This due to the active ingredients present in the *Syzygium cumini* extract of its most abundant Gallic acid nature [11]. When compared with the results of Oral glucose tolerance test; STZ induced diabetic rats by the administration of *Syzygium cumini* extract and phytosome formulation in the present research proved that the phytosome formulation has better results of controlling the diabetes in rats. This could be due to the fast penetration nature of the most abundant Gallic acid present in *Syzygium cumini* in lipoidal biological membrane, and as such the phyto constituents cannot simply get absorbed and their passage through the lipoidal biological membrane.

A known fact, that the biological membrane has a double-layered of lipoidal nature and has poor penetration. The component present in phytosome formulation of cholesterol and lecithin has an affinity for fast penetration in lipoidal bilayer. This proves in our research that the phyto constituents have a drawback that they are restricted in their effectiveness due to their poor absorption and restricted solubility in water [12]. And further supports the earlier literature of the useful role of phospholipids in enhancing the therapeutic efficiency of phytochemicals having poor oral absorption. Phyto somes shows higher absorption since the water soluble constituent is coated by a lipotropic outer layer and thus show higher bioavailability than the traditional herbal extracts [13, 14].

Reference

1. Mac Callum JL, Tieleman DP, Interactions between small molecules and lipid bilayers, Cur. Top. Membr. 2008; 60:227-256.
2. Kareparamban J, Nikam P, Jadhav A, Kadam V. Phytosome: a novel revolution in herbal drugs. International journal of research in pharmacy and chemistry. 2012; 2:299-310.
3. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014; 37(Suppl. 1):S81-S90.
4. Available online at www.ijpsdr.com
5. International Journal of Pharmaceutical Sciences and Drug Research. 2010; 2(4): 224-228
6. Available online at www.ijpsdr.com
7. International Journal of Pharmaceutical Sciences and Drug Research. 2010; 2(4): 224-228
8. Joseph A. Kareparamban, Pravin H Nikam, Aruna P Jadhav and Vilasrao J Kadam. Phytosome: a novel revolution in herbal drugs. IJRPC 2012, 2(2) 299-310.
9. Modi DC, Patel JK, Shah BN, Nayak BS. Pharmacognostic studies of the seed of *Syzygium cumini* Linn. Pharma science monitor an international journal of pharmaceutical sciences. 2010; 1(1):20-26.
10. Bhatia IS and Bajaj KL: Chemical constituents of the seeds and bark of *Syzygium cumini*. Planta Medica. 1975; 28: 346-352.
11. Chopra RN, Nayar SI and Chopra IC: In Glossary of Indian medicinal plants. P.I.D., 1956: 238.
12. OECD, 2001. The Organization of Economic Co-operation Development (OECD), The OECD Guideline for Testing of Chemical: 423- Acute Oral Toxicity – Acute Toxic Class Method. OECD, Paris: 2001; 1–14.
13. Napapach Chaimum-aom, Sanong Chomko, Chusri Talubmook. Toxicology and Oral Glucose Tolerance Test (OGTT) of Thai Medicinal Plant Used for Diabetes control, *Phyllanthus acidus* L. (EUPHORBIACEAE). Pharmacogn J. 2017; 9(1): 58-61.

14. Pal S, Mishra A, Rawat AK, Maurya R, Srivastava AK. Antidiabetic potential of whole plant of *Phyllanthus niruri*. World Journal of Pharmaceutical Research. 2015; 4(5): 1010-1042.
15. Ambika Chauhan and Intelli. *Syzygium cumini* (Jamun): Potential Benefits in Hyperglycemia. SOJ Pharmacy & Pharmaceutical Sciences. 2015; 2(3):1-3.
16. Prasanna Habbu, Smita Madagundi, Rajesh Shastry, Rashmi Vanakudri, Venkatrao Kulkarn. Preparation and Evaluation of Antidiabetic Activity of *Allium cepa*-Phospholipid Complex (Phytosome) in Streptozotocin Induced Diabetic Rats. RGUHS J Pharm Sci. 2015; 5(4):132-141.
17. Formulation and Evaluation of Capsules of *Ashwagandha* Phytosomes. Keerthi B, Prasuna Sundari Pingali, Dr. Prathima Srinivas. Int. J. Pharm. Sci. Rev. Res. 2014; 29(2):138-142.
18. Ahmed N. Allam, Ibrahim A. Komei and Ossama Y. Abdallah. Tailor Made Phospholipid Based Curcumin Phytosomes: Fabrication, Characterization and Ex-Vivo Permeation. 2016:11(3):120-127.