



## Formulation and evaluation of combined herbal tablet of *S. Oblonga linn.* and *E. Littorale blume.* extract

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### Abstract

The aim of the current study was to prepare Combined Herbal Tablet (CHT) from Indian Medicinal Plants whole extracts of *S. oblonga* Linn. stem and *E. littorale* Blume. aerial part. The plants were selected based on extensive literature review, which reflect their utility in treatment of diabetic patients. Wet granulation technique were used for formulation of CHT and assessed according to the Pharmacopoeial guidelines. The preformulation investigation of CHT demonstrated that all the results were within adequate limit. Friability and hardness are important characteristics for disintegration of tablet. Result of the present study had showed hardness of CHT range from  $4.78 \pm 0.71$  to  $5.73 \pm 0.96$  and whereas, %friability ranges from  $0.34 \pm 0.011$  to  $0.88 \pm 0.074$ , indicated that the CHT were mechanically stable. CHT granules displayed excellent to good flow and were compacted into 460 mg tablets. The weight variation test of herbal tablet was passed (mean weight- 468 mg, weight variation  $\leq 5\%$  as per USP). The disintegration time range of CHT was  $13.29 \pm 1.88$  to  $21.02 \pm 2.65$ . The last end drawn from the previously mentioned information is that the conceivable utilization of this economical natural formulation of plant origin might additionally be investigated for antidiabetic potential along with mechanism of action and its long term safety.

**Keywords:** *S. oblonga*, *E. littorale*, anti-diabetes tablet, preformulation study

### Introduction

Diabetes mellitus is a multi-factorial metabolic illness, become more common over the world, and characterized by an increase in blood glucose level caused by either defect in secretion of insulin, abnormalities in action of insulin, or both [1, 2]. The chronic complications of diabetes have become a major cause of morbidity and mortality [3, 4]. Cho *et al* [5] 2018 quotes, there were 135 million diabetics in 1995, and this number is anticipated to rise to 693 million by 2045. Furthermore, a large portion of this rise will occur in developing countries, owing to obesity, population expansion, bad diets, and sedentary lifestyles. Its occurrence more than doubles over the two decades makes it the 5th deadliest disease in the nation and was caused approximately four million deaths globally in 2017 year [6, 7]. The modern synthetic anti-diabetic agents have genuine aftereffect like complication of kidney, liver and haematological effects [8]. Treatment of diabetes imposes a significant financial burden on people and families, as well as national and international health systems [9, 10].

In developing countries, like India where the major portion of population (80%) depends upon the Indian System of Medicines with a belief of low cost, easily availability, and no or less adverse effect [11]. There are several medicinal plants, which are known for their contribution to traditional as well as modern medicines for the treatment of diabetes mellitus. The plants *S. oblonga* and *E. littorale* are among them, plays a vital role in human healthcare. The *S. oblonga* and *E. littorale* are also referred as “Saptrangi” and “Chota-chiretta” respectively and extensively distributed throughout in India. Both the herbs are used to treat hernia, hyperlipidemia, rheumatism, diabetes, abdominal ulcers, insect poisoning, itching, swelling, asthma, inflammation, gonorrhoea and cancer in folk medicines [12, 13, 14]. They are often used singly or in combination. Polyherbal are plant-based formulations, which might apply synergistic, potentiative, agonistic activities by uprightness of its related different dynamic principles [15]. From this point of view, efforts have been made to formulate & evaluate the combined herbal tablet, which are effective and safer alternative to treat diabetes mellitus.

### Material and Methods

#### Plant Materials

The dried plants were collected from the local market and authenticated by Dr. A. Singh, Dhanvantri Ayurvedic College, Mohali. Starch, Dibasic calcium phosphate, lactose, talc, and magnesium stearate, are procured by micro labs, hosur, and from HIMEDIA laboratory, Mumbai, India.

#### Preparation of the Extracts

The dried plants were grinding using mechanical grinder and material pass through a 40-mesh sieve. 200 g coarse powder was extracted with water for 30 minutes at 50°C. The extracts were centrifuged, filtered, and used to dry on the water bath, which was further used for the preparation of combined herbal tablet formulation.

### Formulation of Combined Herbal Tablet

The dried extracts of *S. oblonga* and *E. littorale* (1:1 ratio) were used for the preparation of combined herbal formulation. The combined herbal tablets consist of following:

**Table 1:** Combined Herbal Tablets (CHT) Composition

Ingredients	F1	F2	F3	F4	F5	F6
<i>E. littorale</i> Blume. Extract	200	200	200	200	200	200
<i>S. oblonga</i> Linn. Extract	200	200	200	200	200	200
Di-basic Calcium Phosphate	10	20	30	-	-	-
Lactose	-	-	-	30	20	10
Starch	30	20	10	10	20	30
Talcum powder	10	10	10	10	10	10
Magnesium Stearate	10	10	10	10	10	10
Total Weight (mg)	460	460	460	460	460	460

### Preparation of Granules

The combined herbal tablets granules were processed by wet granulation method. The distilled water was used to prepare starch solutions. Which was further, heated on water to make translucent semisolid mass. The weighed quantities of extracts and other excipients were thoroughly mixed. With continuous mixing, add starch solution to make a damp mass. The mass was passed through 6 number sieve to prepare granules. These granules were dried in an oven for 3 hrs at 60°C temperature. Further, dried granules were passed through 14 number sieve and were subjected to lubrication. Lastly, granules were compressed using single punch tablet compression machine.

### Evaluation of Combined Herbal Granules

#### Preformulation Studies

##### a. Angle of repose <sup>[16]</sup>

The funnel method was used for evaluation of angle of repose. The weighed amounts of combined herbal granule were allowed to flow freely through the funnel. Precautionary measure was given to adjust the height of the funnel in such a distance that the funnel tip just touches the apex of the hill. The periphery of the herbal granules hill was measured and angle of repose was calculated by the following formula:

$$\tan \theta = h / r$$

Where h = height of granules hill,

r = radius of the granules hill

##### b. Loose bulk density <sup>[17]</sup> (LBD)

The bulk density was evaluated by taking a weighed amount of combined herbal granules into a measuring cylinder and quantifying the weight and volume.

Loose Bulk Density = weight of the granules / volume of the packing

##### c. Tapped bulk density <sup>[18]</sup> (TBD)

A weighted quantity of combined herbal granule being placed in a measuring cylinder to calculates the TBD. At two-second intervals, the cylinder was permitted to tap on a hard floor from a specific height (approx. 10 cm). The tapping would go until there was no more change in volume.

Tapped Bulk Density = weight of the granules / volume of granules after tapping

##### d. Compressibility/Carr's index <sup>[19]</sup>

The Carr's index of the combined herbal granules was computed using the following formula:

$$\text{Compressibility index (\%)} = (\text{TBD-LBD}) \times 100/\text{TBD}$$

##### e. Hausner ratio <sup>[20]</sup>

It is a powder flow index and an assessment of the combined herbal granules frictional force. The relationship of tapped density to bulk density has been used to calculate it.

$$\text{Hausner ratio} = \text{TBD} / \text{LBD}$$

##### f. Loss on drying <sup>[21]</sup>

1g granules were correctly weighed and placed to a dried, glass-stopper pre-weighted bottle. The bottle was put on the drying medium. The bottle's stopper was removed, and the entire contents were dried at 100-105°C until a

steady weight was obtained. With respect to the original weight, the percentages loss on drying was derived using the following:

$$\text{Loss on drying (\%)} = [(\text{Initial weight} - \text{Final weight}) / (\text{Initial weight})] \times 100$$

### Evaluation of Combined Herbal Tablet

#### Postformulation Studies

##### a. Weight variation test <sup>[21]</sup>

Twenty CHT were chosen at random. They were each weighed separately to ascertain the mean weight and the percentage variation from the mean. This was done to ensure that the weights of combined herbal tablets are consistent.

##### b. Hardness test <sup>[22]</sup>

It was tested by randomly selecting ten combined herbal tablets. The tablet was held on the tip of the Monsanto Hardness Tester for examination. A hardness of 3-5kg/cm<sup>2</sup> is considered adequate for uncoated tablets.

##### c. Friability test <sup>[23]</sup>

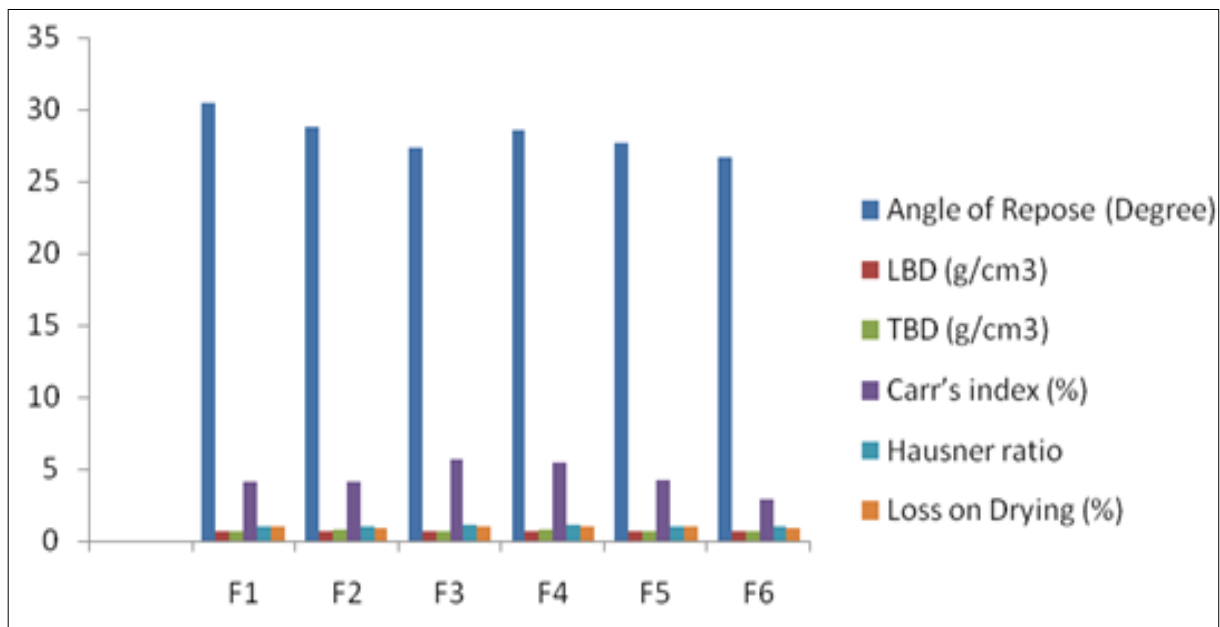
Friability refers to the weight loss of a tablet due to the loss of tiny particles from the surface. Ten pre-weighed combined herbal tablets were rotated at 25 rpm for four minutes in Roche Friabilator. The tablets were again dusted and reweighed.

##### d. Disintegration test <sup>[21]</sup>

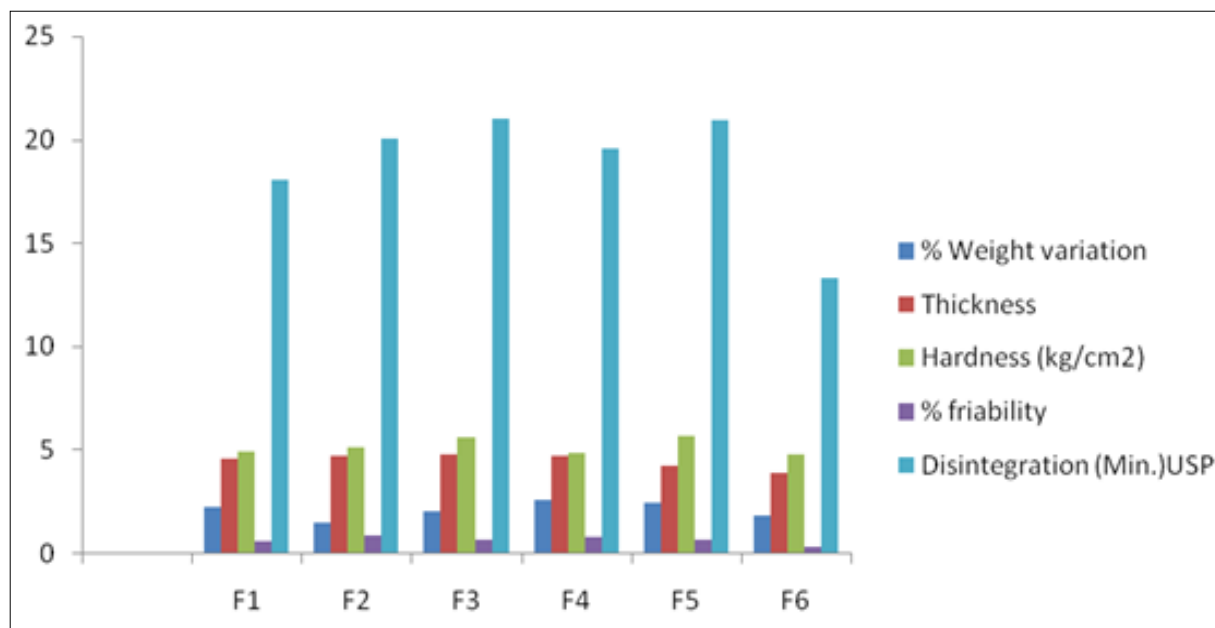
The USP basket type equipment was used to evaluate disintegration. One combined herbal tablet was inserted in each of the 6 tubes of the basket having a plastic disc (80-100 mm length with an inner diameter of about 28 mm and outer diameter 30 mm and rust proof wire gauge [10 mesh screen] at lower end) and the basket rack was submerged in 1 L beaker of water. The water bath temperature was maintained at 37±2° C. The basket was subjected to the up and down movement at a frequency of 28-32 cycles per minute. The time requires to all tablets to disintegrate and pass through wire mesh was noted.

##### e. Thickness <sup>[24]</sup>

It can be determined by using vernier callipers to randomly select ten CHT. All of the readings were taken three times.



**Fig 1:** Preformulation evaluation of combined herbal tablet Granules



**Fig 2:** Evaluation of combined herbal tablet

### Results and Discussion

The combined herbal tablet of aqueous extracts of *S.oblonga* Linn. stem and *E. littorale* Blume. aerial part were formulated and evaluated as per pharmacopoeia parameters. The dried granules of herbal tablet were evaluated for pre-formulation variables includes angle of repose, tapped bulk density, loose bulk density, carr's index, hausner ratio and loss on drying. The results of pre-formulation evaluation of combined herbal granules were given in Table 2. The herbal granules formulated by wet granulation method revealed that all the pre-formulation variables were within the acceptable ranges. The angle of repose is related to the coefficient of interparticle friction by the expression previously given only when the particles are all of the same shape and size [25]. The angle of repose was observed to be in range of  $26.71 \pm 1.44$  to  $30.43 \pm 1.83$ . The best angle of repose was observed for F6 formulation, which showed excellent flow, and the lowest for F1 formulation, which exhibit good flow. For other prepared formulation it was less than  $30^\circ$ , reflect excellent to good flow. The loose bulk density was observed to be in limits of  $0.66 \pm 0.016$  to  $0.70 \pm 0.022$ . The order of LBD was  $F2 \geq F4 > F1 > F5 > F6 > F3$ . The tapped bulk density was observed to be in limits of  $0.69 \pm 0.011$  to  $0.74 \pm 0.015$ . It was found that loose and tapped bulk densities were nearly identical. LBD and TBD are used in calculation of Hausner ratio and Carr's index (%). Carr's index ( $\leq 10\%$ ) and Hausner ratio (1.00-1.11), is a characteristic of excellent flow [26]. All the prepared herbal formulations (F1-F6) indicated the value fall in these permissible limits, indicated excellent flow properties of combined herbal granules. The loss on drying of combined herbal granules ranges from  $0.919 \pm 0.013$  to  $0.977 \pm 0.011$ . F6 formulation showed lowest loss on drying as compred to other formulation.

**Table 2:** Preformulation Evaluation of Combined Herbal Tablet Granules

Formulation/Parameters	Angle of Repose (Degree)	LBD (g/cm <sup>3</sup> )	TBD (g/cm <sup>3</sup> )	Carr's index (%)	Hausner ratio	Loss on Drying (%)
F1	$30.43 \pm 1.83$	$0.69 \pm 0.021$	$0.72 \pm 0.014$	$4.16 \pm 0.74$	$1.043 \pm 0.034$	$0.964 \pm 0.012$
F2	$28.83 \pm 2.08$	$0.70 \pm 0.018$	$0.73 \pm 0.017$	$4.10 \pm 1.01$	$1.042 \pm 0.025$	$0.925 \pm 0.017$
F3	$27.32 \pm 1.67$	$0.66 \pm 0.020$	$0.70 \pm 0.013$	$5.71 \pm 1.26$	$1.060 \pm 0.061$	$0.953 \pm 0.016$
F4	$28.55 \pm 1.85$	$0.70 \pm 0.022$	$0.74 \pm 0.015$	$5.40 \pm 0.91$	$1.057 \pm 0.079$	$0.977 \pm 0.011$
F5	$27.62 \pm 2.17$	$0.68 \pm 0.019$	$0.71 \pm 0.012$	$4.22 \pm 0.88$	$1.044 \pm 0.054$	$0.962 \pm 0.015$
F6	$26.71 \pm 1.44$	$0.67 \pm 0.016$	$0.69 \pm 0.011$	$2.89 \pm 0.87$	$1.029 \pm 0.028$	$0.919 \pm 0.013$

Note: The value are given as Mean $\pm$ SD, (N= 3)

Further, the CHT were evaluated for postformulation variable include thickness, hardness, weight variation friability and disintegration time (Table No.3).

The thickness of herbal tablets was found to between  $3.89 \pm 0.55$  to  $4.82 \pm 0.64$  mm<sup>2</sup>. The Monsanto Hardness Tester was used to determine hardness of herbal tablet. Hardness of herbal tablet was lies in between  $4.78 \pm 0.71$  to  $5.73 \pm 0.96$  kg/cm<sup>3</sup>, which shows a considerable hardness that, will ease to disintegrate the tablets. Herbal tablets (F6) formulation demonstrated noticeable hardness properties ( $4.78 \pm 0.71$ ), resulting in a faster breakdown ( $13.29 \pm 1.88$ ). The force required to compress the tablet is an important parameter need to be taken into consideration while compress the tablet. There is a relationship between hardness and compression force. The tablet disintegration time rises as the compression load increased, but the friability reduces. To manufacture a tablet that satisfies the friability standards, a certain degree of compressive load is required. However, applying

excessively compressive load may not lead to a significant increase in hardness, but it may have a detrimental effect on disintegration and dissolution, which may also induce internal stress cracks, resulting in tablet flaws [27].

The F6 formulation's percent friability ( $0.34\pm 0.011$ ) revealed that the herbal tablet was mechanically stable. Uncoated compressed tablets with a percent friability of between 0.5% to 1% weight losses are regarded as acceptable [28]. As Per USP, the permissible weight variation limit is  $\leq 5\%$ . The mean weight of combined herbal tablets was 468 mg with % weight variation limits  $1.88\pm 0.26$  to  $2.62\pm 0.44$ . Hence, the prepared combined herbal tablet passed the weight variation test. Disintegration is a mechanical process during which a tablet is mechanically breaking down into smaller pieces. As a result, disintegration is the most important step in the dissolution process, following to solubility and bioavailability of the drug molecules [29]. The disintegration time of herbal tablet was ranges from  $13.29\pm 1.88$  to  $21.62\pm 2.65$ . The (F6) formulation had showed lowest disintegration time  $13.29\pm 1.88$ , whereas (F3) formulation had showed  $21.62\pm 2.81$ . All the prepared formulation had passed the limits of disintegration specified by United State Pharmacopoeia [29].

**Table 3:** Postformulation Evaluation of Combined Herbal Tablet

Formulation/ Parameters	% Weight variation	Thickness (mm <sup>2</sup> )	Hardness (kg/cm <sup>2</sup> )	% friability	Disintegration (Min.) USP
F1	$2.26\pm 0.24$	$4.63\pm 0.48$	$4.93\pm 0.35$	$0.63\pm 0.021$	$18.04\pm 1.54$
F2	$1.54\pm 0.74$	$4.74\pm 0.53$	$5.16\pm 0.62$	$0.88\pm 0.074$	$20.07\pm 2.65$
F3	$2.05\pm 0.53$	$4.82\pm 0.64$	$5.63\pm 0.71$	$0.69\pm 0.046$	$21.02\pm 2.81$
F4	$2.62\pm 0.44$	$4.71\pm 0.91$	$4.88\pm 0.85$	$0.81\pm 0.083$	$19.57\pm 2.19$
F5	$2.49\pm 0.71$	$4.26\pm 0.67$	$5.73\pm 0.96$	$0.70\pm 0.029$	$20.98\pm 2.84$
F6	$1.88\pm 0.26$	$3.89\pm 0.55$	$4.78\pm 0.71$	$0.34\pm 0.011$	$13.29\pm 1.88$

Note: The value are given as Mean $\pm$ SD

### Conclusion

Herbal commercial products may comprise a single herb or a mixture of herbs with supportive and/or synergistic effects [30]. Combined herbal tablet pre and post formulation investigations had showed that all of the characteristics assessed were within reasonable bounds. All of the prepared combined herbal granules had a good to excellent flow and had been compressed into 460 mg tablets. In regards of disintegration time, the prepared (F6) herbal formulation outperformed the other five batches. In conclusion, combined herbal tablets formulation of aqueous extract of *S. oblonga* Linn. stem and *E. littorale* Blume. aerial part requires additional research to completely understand the fundamental mechanism of action for diabetes, as well as its long-term consumption consequences.

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