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Access this article online

Website: www.ayujournal.org

DOI: 10.4103/0974-8520.182748

Quick Response Code:

Pharmaceutical Standardization

A contemporary approach on design, development, and evaluation of Ayurvedic formulation - *Triphala Guggulu*

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Abstract

Introduction: Ayurvedic texts describe many formulations for different ailments. *Triphala Guggulu* (TG) is reputed for treating inflammatory conditions. These formulations have been considered complementary medicine or alternative to conventional medicines across the globe. These complex polyherbal formulations need science-based approach toward manufacturing process and chemical standardization. **Aim:** To evaluate TG tablets to meet modern pharmaceutical approaches and also standardization processes. **Materials and Methods:** *Shodhana* of *Guggulu* was performed using *Triphala Kwatha* (decoction) as mentioned in ayurvedic texts. This processed material was dried using spray drying technique, blended with other herbal powders as per formula and using suitable excipients was incorporated for compressing into tablets. Excipients and their concentrations were evaluated for various micromeritic properties and the formula that met the requirements was compressed. **Results:** The angle of repose was considered fair with a range of 25–30, Carr's index at a range between 17 and 30, and Hausner ratio of 1.21:1.44, which was well within the limits as per the United States Pharmacopeia (USP) and among the three blends tested, blend *Triphala Guggulu* formulation-3 was found most suitable for tablets compression. Physical properties were well within the limits as per the USP and disintegration time was within 30 min. **Conclusion:** Modern pharmaceutical processing can very well be adapted for *Guggulu* preparations.

Key words: Ayurvedic formulation, micromeritic properties, process controls, *Triphala Guggulu*

Introduction

Herbs and herbal medicines are preferred by people since ages, and about 80% of the global population still rely on herbs and herbal remedies for chronic ailments.[1] Ayurveda is one of the oldest systems of medicine, which is in practice since ages. Due to globalization and increased awareness, the traditional medicine usage is increasing every year. With an increase in global demand for herbal medicine, it is now important to ensure consistency in quality of products from batch to batch. To achieve this, a contemporary approach to one of the most renowned formulations mentioned in Ayurveda *Triphala Guggulu* (TG) was taken up as a model. This approach will help to control the process parameters during manufacturing.[2-4]

Among the *Guggulu* preparations, TG is one of the widely used preparations. Traditional texts describe in detail about the manufacturing process for the same. However, in modern practice, to fulfill market demand, an industrial approach for the traditional manufacturing process is warranted. Furthermore, with increase in demand globally, there is an unmet challenge to meet global regulations. This underlines the need to translate this *Vati* preparation in modern pharmaceutical dosage forms into pharmacopeial tablet formulation. In the present study, an attempt is made to

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How to cite this article: Muguli G, Gowda VD, Dutta V, Jadhav AN, Mendhe BB, Paramesh R, *et al*. A contemporary approach on design, development, and evaluation of Ayurvedic formulation - *Triphala Guggulu*. Ayu 2015;36:318-22.

adopt TG into a tablet formulation meeting the United States Pharmacopeia (USP) requirements.

Materials and Methods

TG contains following herbs as described – *Guggulu* (*Commiphora wightii* [Arn.] Bhandari) was purchased from Gujarat Medicinal Plants Growers' Society, and other botanical substances such as *Amla* (*Emblica officinalis* Gaertn.) fruit, *Haritaki* (*Terminalia chebula* Retz.) fruit, *Vibhitaki* (*Terminalia bellirica* [Gaertn.] Roxb.) fruit, and *Pippali* (*Piper longum* L) fruit were purchased from local market of Bengaluru, Karnataka, and were authenticated by Botanist of The Himalaya Drug Company, Bengaluru. Excipients such as tapioca native starch (B. No. 12-11-07-A; South East Asia Organic Company, Thailand); Kollidon CL (B. No. 02817168EO; BASF, India); and magnesium stearate (B. No. 125912; Amish Drugs, India) were purchased.

Shuddha Guggulu was prepared using *Triphala* (herbal blend in equal quantities of *E. officinalis*, *T. chebula*, and *T. bellirica* fruits) decoction as per the process mentioned in the Ayurvedic Formulary of India (AFI).[5]

Preparation of *Triphala Guggulu* tablets

Preparation of Triphala Kwatha

Powdered fruit blend (5 kg) was boiled in 40 L of demineralized water for 3 h using extraction vessel with a fixed temperature ranging from 85°C to 95°C. The extract was filtered using 100 μm filter cloth. The filtrate was further used to process *Guggulu*.

Preparation of Shuddha Guggulu

The process involved use 5 kg of *Guggulu* which was tied in 100 μm muslin cloth and suspended in a SS304 vessel containing *Triphala Kwatha*. This vessel was then heated at a temperature between 85°C and 95°C for 3 h. Then, the material was removed, and filtrate (*Shuddha Guggulu*) was spray dried using spray dryer at 180°C as inlet and 110°C as outlet temperature. The dried material was collected in double-lined food grade low-density polyethylene bags, sealed, and stored in high- density polyethylene container. The dried sample was subjected to high-performance liquid chromatography analysis.

Preparation of tablets

Spray dried TG obtained above was formulated using excipient combinations as per Tables 1 and 2.

Compatibility studies

Differential scanning calorimetry (DSC) was performed using Perkin Elmer, DSC 8000, USA. The instrument was calibrated using high purity indium metal as standard. The dynamic scans were taken in nitrogen atmosphere at a heating rate of 10°C min. The runs were made in triplicate. Compatibility between the herbal active and formulation ingredients was done by comparison of decomposition of herbal active alone and in formulation.

Micromeritic properties

The spray dried powder with addition of suitable excipients helped in uniform blending. Before compression, the resultant powder was evaluated for angle of repose, bulk density (Bd), tapped density, Carr's index, and Hausner ratio.[6]

Table 1: Formulation chart (each 750 mg of *Triphala Guggulu*)

Ingredients (mg/tablet)	F1*	F2*	F3*
Triphala Guggulu herbal blend	750	750	750
Tapioca starch	180	210	210
Crospovidone	30	20	30
Magnesium stearate	10	15	-
Crospovidone CL	-	-	10
Colloidal silicon dioxide	30	5	-

*Formulations

Table 2: *Triphala Guggulu* herbal blend details

Botanical name	Quantity (mg/tablet)
Shuddha Guggulu	416.67
Emblica officinalis Gaertn.	83.33
Terminalia chebula Retz.	83.32
Terminalia belerica (Gaertn.) Retz.	83.34
Piper longum L.	83.34

Granulation

The herbal blend, which constitutes dry extract and powdered botanicals with excipients and known quantity of demineralized water, was transferred and mixed using rapid mixer grinder. The material was dried in a fluid bed dryer at a controlled temperature of 60–70°C till the material achieved moisture of <5% and then subsequently was milled and sifted through 20# sieve. The retained material on the sieve was passed through multimill and passed through 20# again.

Tablets compression

The three formula excipient blends were developed and evaluated for micromeritic properties; based on the results of micromeritic properties of these herbal blends, finally, blend-T3 was taken for tablet compression. Compression was performed on Cadmach 16 [Cadmach Machinery Co. Pvt. Ltd, Ahmedabad, Gujarat, India] station punching machine with rpm of 18 and pressure of 4–5 kg.

Evaluation of tablet properties

Uniformity of weight

Randomly sampled tablets (10 numbers) were weighed individually on a precision balance. The average weights were determined.[7]

Crushing strength

Monsanto hardness tester was used to determine tablet hardness. Ten tablets were chosen randomly and force needed for each of the tableting runs and the average values were determined.

Disintegration time

Tablet disintegration test was performed employing disintegration tester using demineralized water at 37 ± 2°C. The time required for complete disintegration of tablets was determined by visual observation.

Friability

Friability of tablets was determined by weighing 10 tablets. These were de-dusted prior testing in an analytical balance and moved for 4 min in a friability tester with a set at a speed of 25 rpm. All loose dust was removed from the tablets. They were reweighed and the percentage friability was calculated and recorded.

Thin-Layer chromatography Thin layer chromatography finger printing of *Triphala Guggulu* tablets with markers

Samples were prepared in methanol (20 mg/ml, for standard - 1 mg/ml) and were filtered through Whatman filter paper. Filtrates were applied on precoated silica gel GF^{254} plate (Merck) by Linomat V (Camag) using 100 µL syringe. Plate was developed in a mobile phase of toluene:ethyl acetate:formic acid:methanol (3:3:0.8:0.5 v/v/v/v). Developed plate was visualized and photographed in ultraviolet light at 254 nm and 366 nm using Camag Reprostar 3, Camag. The plate was derivatized with vanillin-sulfuric acid reagent and heated at 105°C for 10 min and then viewed under white light [Figure 1]; the R_f values were 0.56, 0.75, 0.76, and 0.74 for gallic acid, guggulsterone-E, guggulsterone -Z, and piperine, respectively.[7]

Results

From the spray drying operation, *Triphala Kwath* processed *Guggulu*, free-flowing powder, was obtained. This was blended with the excipients and DSC carried on this blend indicated [Figures 2 and 3] that there is no interaction between the excipients and proposed tablet actives. Powder characteristics are vital for solid dosage forms and the result of micromeritic properties of these blends is summarized in Table 3. Tablets made from the blend *Triphala Guggulu* formulation (TGF)-3 were evaluated for tablet weight uniformity, crushing strength, disintegration test, and friability [Table 4].

Discussion

In the classical preparations of *Guggulu*, different processing methods for different preparations are mentioned. Drying process impacts the quality of the formulation, and hence, practical implementation of these practices at commercial manufacturing needs critical process control parameters. Monitoring these parameters will help to control batch to batch variations. In the present study, we have used spray drying technology for drying of processed *Guggulu*. Use of this technology allows to control powder characteristics (for example - Bd, moisture, flow properties, etc.) and uniform formulation can be developed batch after batch. The powder blends were evaluated for compatibility studies by

Table 3: Micromeritic properties of formulation blends of *Triphala Guggulu*

Formulation	Angle of repose* (θ)	Bulk density* (g/cm³)	Carr's index* (%)	Hausner ratio*
TGF-1	44.80±1.04	0.52±0.00	27.5±1.51	1.37±0.01
TGF-2	37.00±0.90	0.57±0.01	17.5±1.04	1.21±0.01
TGF-3	29.22±1.08	0.67±0.01	12.3±1.03	1.15±0.01

*n=5. Values expressed as mean±SD. TGF: *Triphala Guggulu* formulation, SD: Standard deviation

Table 4: Results of pharmaceutical evaluation of *Triphala Guggulu* tablets

Evaluation parameter	Mean±SD*
Average weight (g)	1.020±0.65
Hardness (kg)	5.17±6.25
Disintegration time (min)	18±0.84
Friability#	0.83±0.45

*n=10, #n=5. SD: Standard deviation

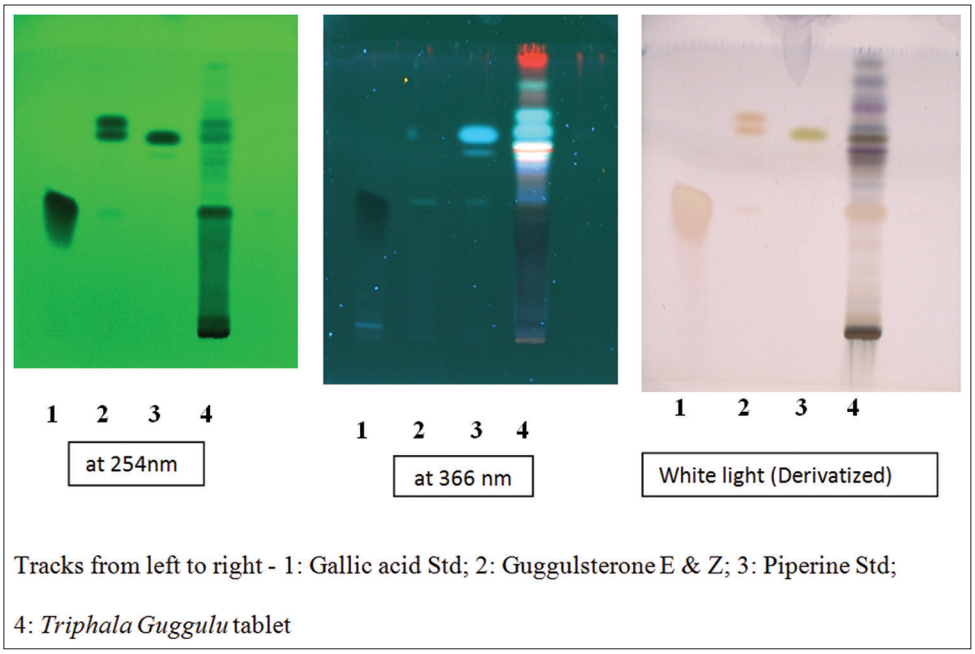

Figure 1:Thin-layer Chromatography profile of *Triphala Guggulu*

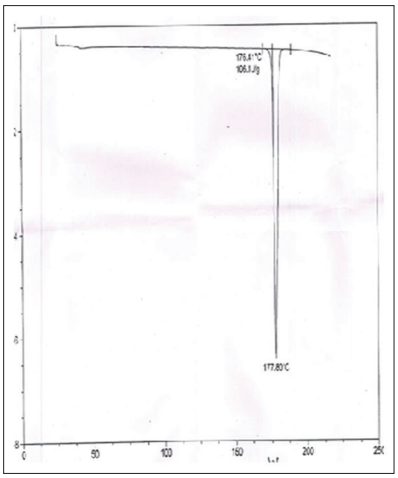

Figure 2: Differential scanning calorimetry of herbal blend of *Triphala Guggulu*

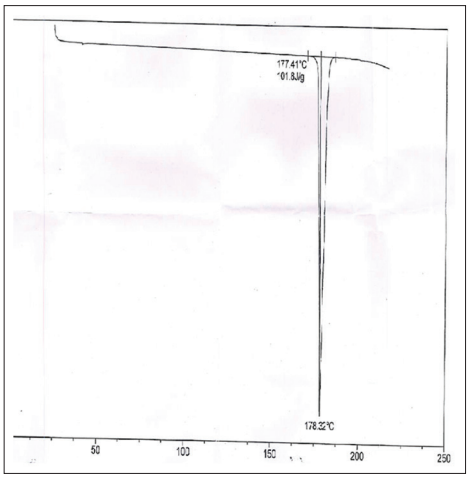

Figure 3: Differential scanning calorimetry of granules of *Triphala Guggulu*

DSC [Figures 2 and 3] which indicated the absence of any interaction between TG and excipients.

USP informs about the limits for powder flow properties, which helps for evaluating the flowability of powders, which is intended for compression into tablet dosage form. Using approved excipients in different combinations, we were able to achieve the required flow property [Table 3] as per USP. Based on these results of micromeritic properties, blend TGF-3 was selected for compression.

Compressed tablets were evaluated for their physical tablet characteristics and found to meet the USP requirements [Table 4]. Interestingly, the tablet disintegration time was <30 min and was pharmaceutically well within limit. This preparation is from *Guggulu* and hence is expected to show higher disintegration time. The Ayurvedic Pharmacopoeia of India (API) limit is of maximum 60 min and the presence of markers such as guggulsterone and piperine is ascertained using thin layer chromatography profile in both before and after derivatization.

Conclusion

Ayurvedic medicines are time tested and have capability to fulfill global requirements of wellbeing. In the current study, oleo-gum-resin of *C. wightii* is the major ingredient and possesses challenge for formulator as it increases the disintegration time of tablet. However, using the modern techniques of spray drying, the TG preparation was converted into free-flowing powder and developed into tablet dosage form meeting modern day regulations. This exercise can well be applied to other *Guggulu* formulations too.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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हिन्दी सारांश

त्रिफला गुग्गुलु का आधुनिक दृष्टीकोण द्वारा रचना, विकास तथा मानकीकरण

गणेश मुगुली, विशकांते गौडा डी., विष्णु दत्ता, अतुल एन. जाधव, बिभीलेष बी. मेंढे, रंगेश परमेश, बाबू यु.वी.

आयुर्वेद में विविध व्याधियों के लिए अनेक सूत्रीकरणो का उल्लेख किया गया है जिसमे से त्रिफला गुग्गुलु दाहनाशकता के लिए प्रख्यात है। संपूर्ण विश्व में इन सूत्रीकरणों को मानार्थ औषधि या परम्परागत औषधि के विकल्प के रूप में जाना जाता है। इन जटील बहुजड़ीबूटीयूक्त सूत्रीकरणों के उत्पादन के लिए वैज्ञानिक तौर पर इनका मानकीकरण करना आवश्यक है। इस अध्ययन का मुख्य उद्देश्य त्रिफला गुग्गुलु वटीका का आधुनिक द्रव्यशास्त्र प्रस्तावों द्वारा मानकीकरण करना। आयुर्वेद ग्रंथानुसार त्रिफला क्वाथ (काढ़ा) के द्वारा गुग्गुलु का शोधन (शुद्धीकरण) किया गया। इस परिष्कृत गुग्गुलु को स्प्रे ड्राईंग तकनीक द्वारा निर्जलित किया गया। इस शुद्ध गुग्गुलु सार की अन्य जड़ी-बूटीयों के चूर्ण के साथ सूत्रानुसार मिश्रित कर उसमे उचित संघटक, जिसका कोई औषधिय उपयोग नही मिलाया गया ताकि उसे गुटीका (वटीका) में अविस्तीर्ण किया जा सके। विविध सूक्ष्मकण गुणधर्मो के आधार पर संघटक एवं उनकी मात्रा का परिक्षण किया गया जो कि निर्धारित सूत्रानुसार पाये गये और उनका अविस्तीर्ण किया गया। एँगल ऑफ रिपोज (सीमा २५-३०), कार्स इंडेक्स (सीमा १७-३०) एवं हस्नर रेशो (अनुपात) (सीमा १.२१-९.८८) जो कि युनाईटेड़ स्टेट फार्माकोपीया (संयुक्त राष्ट्र संघ भेषझग्रंथावली) के प्रमाणकी पर खरी पायी गयी। परखे गये तीनो मिश्रणों में से मिश्रण टीजीएफ- ३ गुटीका (वटीका) दबाव प्रक्रिया के लिए अत्यंत उपयुक्त पायी गयी। भौतिक गुणधर्म परिक्षण, यु.एस.पी. द्वारा निर्धारित सीमांतर्गत अनुकुल पाया गया और गुटीका (वटीका) का विघटन समय ३० मिनीटों के भीतर पाया गया। प्रस्तुत आधुनिक द्रव्यशास्त्र प्रक्रिया की गुग्गुलु मिश्रित औषधि निर्माण के लिए अनुकुल माना जा सकता है।