Research Article

# Formulation and Evaluation of Triphalaguggulkalpa Tablets for Optimum Disintegration Time

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**ABSTRACT**

Apart from anti-inflammatory and other pharmacological actions, *guggul* is used as a binder in ayurvedic tablet formulations. Prior to incorporation into formulations, *guggul* is subjected to *shodhana* process. Earlier experiments on marketed *triphalaguggulkalpa* tablets exhibited delayed *in vitro* disintegration that might be attributed to *shodhana* of *guggul*. The study was focused at standardization of *triphalaguggulkalpa* tablets, an ayurvedic preparation, consisting of *guggul*. The main objective was to determine the effect of *shodhana* process on performance characteristics, namely, disintegration time and hardness of tablets. The study was aimed at optimization of the *shodhana* process. The study involved *shodhana* of *guggul* with *triphalaquath*, preparation of *triphalaguggulkalpa* tablets by direct compression, and evaluation of the *triphalaguggulkalpa* tablets. The *shodhana* process was optimized using 3×2 factorial design. The independent variables were volume of *triphalaquath* and the contact time of *triphalaquath* with *guggul*. The dependent variables were disintegration time and hardness of tablets. The preliminary and factorial batches of *triphalaguggulkalpa* tablets, having different lots of *shodhitguggul*, revealed considerable variations in disintegration time and hardness of tablets. Increasing the volume of *triphalaquath* resulted in higher disintegration time and hardness. The mixing time has a complex role in controlling the tablet hardness and disintegration time. The study determined optimum conditions for *guggul* (10 gm)- 20 ml of *triphalaquath* and 20 hour contact time- during *shodhana* process. The findings provided experimental evidence that *shodhana* process controlled the binding and disintegrating properties of *guggul*, in turn controlled the hardness and disintegration of *triphalaguggulkalpa* tablets.

**Keywords:** optimization, shodhana, binder, disintegration time, Ayurveda.

## INTRODUCTION

Therapeutic use of ayurvedic medicines and dosage forms is preceded by shodhana process.[1] The shodhana treatment was frequently utilized by the pioneers of Rasashastra especially for the purification of mineral/herbomineral drugs, without affecting their medicinal properties.[2] The objectives of shodhana are removal of impurities, facilitation of further processing of dosage form, sukshmikarana of drug, augmentation of the potency of the drug.[3] During shodhana, mineral/ herbo-mineral drugs are subjected to grinding, heating, fomentation, sublimation, distillation for removal of soluble, evaporable and washable impurities. The mineral/ herbo-mineral drugs are treated with acidic, alkaline and neutral types of vegetable extracts/liquids/oily materials, at room temperature or heated, for a specified period of time.[4]

There are few attempts of systematic study for understanding the importance of shodhana process.[4-7] The effect of vegetable extracts/liquids/oily materials, employed during shodhana, of *Commiphora wightti* Arn[3], *Dhattura metal* Linn[8], *Aconitumm ferox* Wall[8], *Strychnos nuxvomica* Linn[8], *Acorus calamus* Linn[9] was reported. Jaiswal et al[10] compared three detoxification strategies of Aconitum heterophyllum Wall, comprising of shodhana treatment with cow milk and cow urine, and treatment with aqueous decoction, a Traditional Chinese Medicine process. All the three methods of detoxification were efficient in detoxification.

Ayurveda describes guggul as an antiseptic, anti-bacterial, astringent, anti-spasmodic, as a carrier for other drugs.[1] Allopathy confirms anti-inflammatory and hypolipedaemic actions of guggul.[11-13] For improving shelf life, churnas (powders) are converted into gutikas (tablets). Guggulkalpa means tablets that contain equal/more amount of guggul as compared to amount of other ingredients.[14,15] Ayurvedic textbooks describe formulae and method of preparation of triphalaguggulkalpa, punarnavaguggulkalpa and shatavariguggulkalpa tablets.[16] Prior to incorporation into formulations, guggul is subjected to shodhana by two ways namely, general purification (with hot water) and specific purification (with triphalaquath, guduchiquath, dashmulaquath, cow's milk).[17] Apart from medicinal uses, ayurveda suggests guggul as a binder in gutikas.[14]

Tablets, the dosage form similar to ayurvedic gutikas, are manufactured by applying pressure to a powder bed. The powder bed may consist of either primary particles or aggregated primary particles (i.e. granules). The properties of the tablet (mechanical strength, disintegration time and drug release characteristics) are affected by both the properties of the excipients and the

manufacturing process. Binders, an important class of excipient added to tablet formulation, are used for their cohesive and adhesive properties to produce granules, tablets. Ideally, binders must give excellent properties such as flowability to the grain, hardness to the tablets and are not to hold up disintegration of tablet.[18] Binders are used both as a solution and in dry form. The same amount of binder in solution is more effective than if it is dispersed in a dry form and moistened with the solvent.[19]

Earlier experiments on marketed triphalaguggulkalpa tablets[20] exhibited delayed *in vitro* disintegration that might be attributed to shodhana of guggul. The main objective was to determine the effect of shodhana process on performance characteristics namely, disintegration time and hardness of triphalaguggulkalpa tablets. The study was aimed at optimization of the shodhana process, by using 3×2 factorial design.

## MATERIALS AND METHODS

Guggul (*Commiphora mukul*) was obtained from the local market, haritaki powder (*Terminalia chebula*), amalki powder (*Emblica officinalis*), bibhitaki powder (*Terminalia belerica*), pippali powder (*Ficus benjamin*), were purchased, as "coarse powders" from the local market. They were dried in shade, packed in airtight containers, and stored at ambient temperature. All other reagents used were of analytical grade.

### Shodhana of Guggul

Haritaki, amalaki, bibhitaki powders and guggul were characterized, before study.[11,21,22] The powders were passed through sieve no 44, weighed in equal amount and mixed. The powder mixture (1 part) was boiled with distilled water (16 parts) till the volume was reduced to one-eighth of its original volume. It was filtered through a muslin cloth. The filtrate, triphalaquath, was used for shodhana of guggul.[15,16]

Guggul was cut into small pieces and foreign organic matter was removed manually as far as possible. Guggul (10 gm) and warm triphalaquath (80 ml), in the ratio 1:8, were mixed thoroughly and allowed to stand for 24 hours.[16,17] The mixture was filtered through a muslin cloth. The filtrate was collected and water was evaporated in an oven, at a temperature not exceeding 60° C, to obtain shodhitguggul.

### Formulation of Preliminary Batches of Triphalaguggulkalpa Tablets

**Table 1:** Formulation of Triphalaguggulkalpa Tablets

| Ingredients | Quantity (mg )/ Tablet |
|---|---|
| Shodhitguggul | 165 |
| Triphala powder | 100 |
| Pippali powder | 33 |
| Talc | 8.4 |
| Magnesium stearate | 2.6 |

Triphalaguggulkalpa tablets[23] were prepared by direct compression. [Table 1]

Initially pippali powder, triphala powder, and shodhitguggul were mixed in 1:3:5 ratio to obtain a coherent mass.

The coherent mass was passed through sieve # 14 and triphalaguggulkalpa granules were dried in hot air oven at a temperature not exceeding 60° C.

Magnesium stearate and talc were passed through sieve #100.

Triphalaguggulkalpa granules were sifted through sieve # 25 and were mixed with talc and magnesium stearate for 15 minutes in a plastic bag to make a uniform blend.

The uniform blend was directly compressed (KarnavatiRimek Mini Press II).

The tablet press setting was kept constant throughout[20] the manufacture of all batches.

The preliminary batches of triphalaguggulkalpa tablets (B1-B8) were prepared with different lots of shodhitguggul by varying the volume of triphalaquath (20, 40, 60 and 80 ml) and the time of contact of triphalaquath with guggul (6, 12, 18 and 24 hours).

### Evaluation of Preliminary Batches of Triphalaguggulkalpa Tablets

The tablets were evaluated for appearance, weight variation, thickness, hardness, friability and disintegration time.[24,25]

Disintegration time was measured in distilled water at 37± 1°C using a tablet disintegration test apparatus (Remiequipments, Mumbai).

The tablets were considered as completely disintegrated when all particles pass through the wire mesh.

### Optimization of Triphalaguggulkalpa Tablets

In the present study, a $3^2$ full factorial design, comprising of 2 factors evaluated at 3 levels was employed for determination of optimum conditions applicable to shodhana of guggul.[25]

The formulation variables and the ranges were chosen from the knowledge acquired from the preliminary batches of the tablet.

The volume of triphalaquath ($X_1$) and contact time of triphalaquath with guggul ($X_2$) were selected as independent (factors) variables.

The independent variables were studied at three levels [Table 2] and nine formulations were formulated [Table 3].

The dependent (response) variables namely, *in vitro* disintegration time of tablet (Y1) and hardness of tablet (Y2), were recorded.

**Table 2:** Factors and Levels in 3×2 Factorial Design Batches

| Coded values | Actual values | |
|---|---|---|
| | $X_1$ (Volume of triphalaquath in ml) | $X_2$ (Contact time of guggul with triphalaquath in hrs) |
| -1 | 10 | 16 |
| 0 | 15 | 18 |
| 1 | 20 | 20 |

**Table 3:** Experimental Design

| Formulation code | Coded values | |
|---|---|---|
| | $X_1$ | $X_2$ |
| F1 | -1 | -1 |
| F2 | -1 | 0 |
| F3 | -1 | +1 |
| F4 | 0 | -1 |
| F5 | 0 | 0 |
| F6 | 0 | +1 |
| F7 | +1 | -1 |
| F8 | +1 | 0 |
| F9 | +1 | +1 |

The factorial batches of triphalaguggulkalpa tablets (F1-F9) were prepared with different lots of shodhitguggul by varying the volume of triphalaquath (10, 15 and 20 ml) and the time of contact of triphalaquath with guggul (16, 18 and 20 hours).

Triphalaguggulkalpa tablets were prepared by the procedure described in Formulation of preliminary batches of triphalaguggulkalpa Tablets.

The data was treated using Stat Ease Design Expert 7.1.6 software and analyzed statistically using analysis of variance (ANOVA).

All the response variables were fitted to a quadratic model and a regression analysis was performed to get a correlation in between the independent and the dependent variables.

The polynomial equation was generated with the help of software.

The data was also subjected to the 3-D response surface methodology to study the interaction of $X_1$ and $X_2$ on dependent variables.

## RESULTS AND DISCUSSION

### Shodhana of Guggul

Haritaki, amalaki, bibhitaki powders and guggul complied with Pharmacopoeial specifications, limit for microbial contamination, and limit for pesticide residue.[11,21,22] (Results not revealed)

Shodhitguggul was sticky in nature. Hence additional binder or any granulating agent or moistening agent was not used during further step.

It was concluded that shodhana of guggul imparted cohesiveness to guggul and confirmed binding properties of guggul.

### Formulation of Preliminary Batches of Triphalaguggulkalpa Tablets

Triphala powder and guggul were lacking satisfactory cohesive and flow properties respectively.

Cohesiveness and flowability are the requirements of direct compression.

Hence direct compression method was modified during initial stages.

Triphalaguggulkalpa granules were prepared by mixing shodhitguggul (5 parts) with triphala powder (3 parts), pippali powder (1 part) and sieving the cohesive mass.

As a binder guggul would surround or coat triphala and pippali powder, thereby forming an easily compressible powder admixture.[26]

Guggul was the major component of the tablet formulation.

The excipients namely, talc or magnesium stearate, were incorporated in triphalaguggulkalpa tablet formulation in minimum quantity.

Hence talc or magnesium stearate exerted less significant effect on the performance characteristics of triphalaguggulkalpa tablets.

The preliminary batches of triphalaguggulkalpa tablets (B1-B7) were prepared with an objective of evaluation of guggul as a binder.

For evaluation of binder, the effect of three parameters namely, 1) concentration of binder in dry form, 2) concentration of wetting liquid, 3) mixing time of binder with wetting liquid, on disintegration time and hardness of tablets should be determined.[26]

In our study, guggul was used as a binder, triphalaquath was used as a wetting liquid and the time period, for which guggul was soaked with triphalaquath during shodhana process, was considered as mixing time of binder with wetting liquid.

Guggul (10 gm) was kept constant since guggul was used for its pharmacological actions whereas the volume of triphalaquath and the mixing time during shodhana process were changed from 20 to 60 ml and from 6 to 24 hours respectively to study the effect of volume of wetting liquid and of mixing time on triphalaguggulkalpa tablets.

### Evaluation of Preliminary Batches of Triphalaguggulkalpa Tablets

Triphalaguggulkalpa tablets, from all the batches, were brownish in color; however the color intensity varied amongst the batches.

The preliminary batches of triphalaguggulkalpa tablets, having different lots of shodhitguggul, revealed considerable variations in disintegration time and hardness of tablets. [Table 4]

**Table 4:** Evaluation of Preliminary Batches of Triphalaguggulkalpa Tablets

| BATCH CODE | Disintegration Time (min)* | Hardness ($kg/cm^2$)** | Friability (%) | Tablet Thickness (mm) | Tablet Diameter (mm) | Tablet Average Weight (mg) |
|---|---|---|---|---|---|---|
| B1 (20ml) | 66.93 ± 1.62 | 3.06 ± 0.11 | 0.177 | 4.54 ± 0.062 | 8.21 ± 0.012 | 281.5 ± 5.87 |
| B2 (40ml) | 82.81 ± 1.62 | 3.26 ± 0.11 | 0.176 | 4.55 ± 0.058 | 8.21 ± 0.013 | 280 ± 5.61 |
| B3 (60ml) | 99.51 ± 1.68 | 3.33 ± 0.11 | 0.176 | 4.56 ± 0.046 | 8.21 ± 0.010 | 279.5 ± 6.04 |
| B4 (80ml) | 111.34 ± 2.02 | 3.46 ± 0.11 | 0.176 | 4.54 ± 0.049 | 8.21 ± 0.013 | 280.5 ± 5.10 |
| B5 (6 hrs) | 95.30 ± 2.50 | 3.33 ± 0.11 | 0.179 | 4.54 ± 0.053 | 8.20 ± 0.013 | 282 ± 5.52 |
| B6 (12hrs) | 106.85 ± 3.85 | 3.46 ± 0.11 | 0.176 | 4.56 ± 0.041 | 8.20 ± 0.011 | 280 ± 6.48 |
| B7 (18hrs) | 63.5 ± 2.27 | 3.46 ± 0.23 | 0.177 | 4.54 ± 0.039 | 8.20 ± 0.011 | 281 ± 5.52 |
| B8 (24hrs) | 113.82 ± 1.42 | 3.48 ± 0.65 | 0.174 | 4.56 ± 0.027 | 8.20 ± 0.0113 | 282 ± 6.91 |

*Each observation is an average of 3 readings

Disintegration time and hardness of triphalaguggul tablets depicted a direct relationship with the volume of triphalaquath and inverse relation with the mixing time of triphalaquath with guggul. It indicated the change in binding properties of guggul during shodhana process. It suggested that variations in the volume of wetting liquid and the contact time of wetting liquid with the binder affected the binding properties of guggul in turn affected disintegration time and hardness of tablets.

The thickness, diameter and average weight did not vary considerably for the tablet formulations. [Table 4] This may be attributed to constant operating conditions during compression of tablets. It indicated adequate process control.

The optimum hardness/disintegration ratio of a tablet is observed by controlling the properties of a binder.[27] Batches B1 and B7 exhibited the least disintegration time (66.93 and 63.5 min respectively) with adequate hardness and friability. The study of preliminary batches revealed that the volume of triphalaquath- 20 ml and the contact time of triphalaquath with guggul- 18 hours, during shodhana process, resulted into best hardness/disintegration ratio. Hence in factorial design experiments, the levels of volume of triphalaquath were fixed at 10, 15 and 20 ml where as the levels of for contact time were fixed at 16, 18 and 20 hours.

**Optimization of Triphalaguggulkalpa Tablets**

The factorial batches of triphalaguggulkalpa tablets indicated the disintegration time and tablet hardness values were strongly dependent on the selected independent variables. [Table 5]

**Table 5:** Evaluation of factorial batches of triphalaguggulkalpa tablets

| Batch Code | Disintegration Time (min)* | Hardness ($kg/cm^2$)* |
|---|---|---|
| F1 | 96.41 ± 0.425 | 3.56 ± 0.08 |
| F2 | 92.11 ± 0.051 | 3.52 ± 0.10 |
| F3 | 89.13 ± 0.075 | 3.48 ± 0.10 |
| F4 | 87.17 ± 0.170 | 3.44 ± 0.08 |
| F5 | 83.25 ± 0.273 | 3.4 ± 0.14 |
| F6 | 77.9 ± 0.302 | 3.32 ± 0.10 |
| F7 | 75.32 ± 0.268 | 3.28 ± 0.10 |
| F8 | 62.13 ± 0.135 | 3.12 ± 0.10 |
| F9 | 57.11 ± 0.045 | 3.12 ± 0.10 |

*Each observation is an average of 3 readings

A statistical model incorporating interactive and polynomial terms was utilized to evaluate the responses.

**Effect of independent variables on disintegration time:**

The regression equation obtained for the disintegration time (D. T.) is as follows:

Final equation in terms of Coded Factors for disintegration time:

$$D.\ T. = 81.88 - 13.85X_1 - 5.79X_2 - 2.73X_1X_2 - 4.07X_1^2 + 1.34X_2^2 \quad \text{(Equation 1)}$$

Final equation in terms of Actual Factors for disintegration time:

D. T. = 73.9502 + 7.0348 × volume of triphalaquath – 10.8879 × contact time – 0.2732 volume of triphalaquath × contact time – 0.1628 (volume of triphalaquath)$^2$ + 0.3358(contact time)$^2$ (Equation 2)

**Effect of independent variables on tablet hardness:**

The regression equation obtained for the tablet hardness (T. H.) is as follows:

Final equation in terms of Coded Factors for tablet hardness:

T. H. = 3.38 – 0.17$X_1$ – 0.060$X_2$ – 0.020$X_1X_2$ – 0.037$X_1^2$ + 0.013$X_2^2$ (Equation 3)

Final equation in terms of Actual Factors for tablet hardness:

T. H. = 4.6377 + 0.0460 × volume of triphalaquath – 0.210 × contact time – 2.00 volume of triphalaquath × contact time – 1.4666 × (volume of triphalaquath)$^2$ × 3.333(contact time)$^2$ (Equation 4)

The results depicted that the disintegration time and hardness of triphalaguggulkalpa tablets was strongly influenced by the variables selected for the study. The same was reflected by the wide range of coefficients of the terms $X_1$ and $X_2$ in Equation 2 and 4. The main effects of $X_1$ and $X_2$ represent the average result of changing one variable at a time from its low level to its high level. The interaction terms ($X_1X_2$, $X_1^2$, $X_2^2$) revealed the changes in disintegration time and tablet hardness with simultaneous changes in two variables. Positive coefficient of $X_1$ (volume of triphalaquath) indicated favorable effect on disintegration time and tablet hardness, while the negative coefficient of $X_2$ (contact time of triphalaquath with guggul) indicated unfavorable effect on disintegration time and tablet hardness. The value of correlation coefficient ($r^2$) of Equation 2 and 4 was 0.9915 and 0.9986 indicating good fit.

From the response surface plot [Figure 1, 2] it was concluded that more the volume of triphalaquath ($X_1$) and the contact time of triphalaquath with guggul ($X_2$), the disintegration time and hardness of triphalaguggulkalpa tablet was less.

On the basis of $3^2$ factorial study, batch F9 was considered as an optimum batch with disintegration time of 57.11 ± 0.045 minute and hardness of 3.12 ± 0.109 Kg/cm$^2$. Batch F9 consisted of shodhitguggul prepared with 20 ml of triphalaquath and 20 hour contact time during shodhana process.

The optimization study involved guggul as a binder, triphalaquath as a wetting liquid and the mixing time of guggul with triphalaquath as the contact time. Guggul quantity (10 gm) was kept constant throughout the experimentation since guggul was mainly used for therapeutic action whereas volume of triphalaquath and mixing time were changed. It was observed that 20 ml of triphalaquath and 20 hour contact time were optimum conditions for shodhana of guggul. [Table 5]

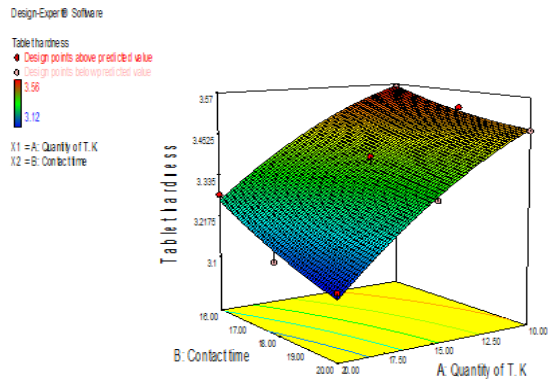


**Figure 1:** Response surface plot for disintegration time

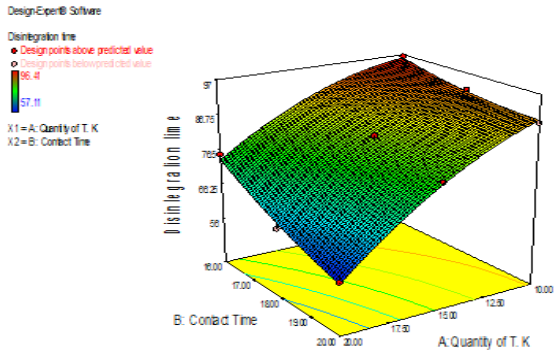


**Figure 2:** Response surface Plot for hardness

It was concluded that guggul acquired adequate cohesive and disintegrant properties at these conditions during shodhana process. According to Chebali[27], the same excipient can exhibit both properties, binding and disintegration, depending upon the degree of crosslinking. It was concluded that the said experimental conditions imparted desired degree of cross linking to guggul, in turn cohesive properties essential for a binder.[17]

The mechanism of disintegration of guggul can be explained as follows. Guggul, a gum oleoresin, being insoluble in nature, absorbs water rapidly without increase in void space. After absorption of water, it swells rapidly thus breaking the interparticle bonds easily and quickly. Thus guggul produces rapid disintegration of the tablet.[27]

## CONCLUSION

The use of experimental design had enabled us to study the influence of volume of triphalaquath (wetting liquid) and the contact time of triphalaquath with guggul (mixing time) employed during shodhana of guggul. Increasing the volume of triphalaquath (from 20 to 80 ml) resulted in higher disintegration time and hardness. The mixing time has a complex role in controlling the tablet hardness and disintegration time. The study determined optimum conditions for guggul (10 gm)- 20 ml of triphalaquath and 20 hour contact time during shodhana process. The findings provided experimental evidence that shodhana process controlled the binding and disintegrating properties of guggul, in turn controlled the hardness and

disintegration of triphalaguggulkalpa tablets. This study would be useful in optimizing other guggulkalpa tablets.

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