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# Formulation and quality evaluations of tulsi tea tablets - a tea diversification product

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## ABSTRACT

This article reports the formulation and quality evaluations of tulsi tea tablets prepared for better applicability. Tulsi-tea extracts (TTE) were prepared by mixing black tea: tulsi in the w/w ratios of 70:30 and tablets were formulated by a combination of wet granulation and direct compression. Micromeritic properties of the powder blend of TTE and excipient was carried out prior to tablets compression followed by post compressional evaluations. TTE and excipient mixed powder blend exhibited excellent flow properties. Post compressional evaluations showed that the formulated tablets are compliant with the pharmacoepial specifications. Batch F3 formulation is considered to be the optimized batch with zero order release kinetics and anomalous flow behavior; TTE release from the formulations is said to follow erosion mechanism. The formulations were stable enough as evident from the results of stability studies. The tablets prepared were satisfactory in terms of quality aspects and aided in better applicability of tulsi-tea extract.

**Keywords**: Tulsi tea extract, Active ingredient, Wet granulation, Micromeritic properties, Post compressional evaluations, Direct compression, Zero order release kinetics, Erosion mechanism

## INTRODUCTION

Despite tremendous strides in modern medicine, prevention and treatment of chronic ailments with physiologically active food components or beverages also known as functional foods as well as dietary supplements is of revived interest in the present health conscious world. The concept of applying functional foods and dietary supplements as adjunct therapy dates back 2,500 years ago when Hippocrates, the father of modern medicine insisted on "Let food be thy medicine and medicine be thy food." Nutraceuticals have already captured the global market and US has already a well established market for botanical dietary supplements (Cygnus Business consulting & Research, 2008), India and China likely adopting the trend. The constant escalations in the number of type 2 diabetics worldwide pose a serious threat to human health and global economies [1-3].

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Immediate adoption of preventive and curative measures to control this chronic metabolic disorder deserves attention. Considering the pathophysiology of type 2 diabetes, along with the use of synthetic drugs under western classical medicine parallel implementations of herbal or dietary supplements is expected to provide a better therapeutic outcome. Tea (*Camellia sinensis*) is a popular beverage consumed throughout the world from time unknown. Black tea is more preferred in Indian context than other varieties and its multifaceted health potentials have drawn research limelight [4]. Nutraceutical products in the form of tablets, capsules or packed powders are the 21$^{st}$ century health boosters. Value addition in tea and tea diversification products has started making their places in health market [5, 6]. Tulsi (*Ocimum sanctum*) is known for its diversified pharmacological actions and is really regarded as the "elixir of life"[3]. Incorporation of tulsi leaf in black tea suggests an effective value addition and can be targeted for Type 2 diabetes. This research paper reports the development of conventional release tablets with tulsi incorporated black tea processed extracts (TTE) followed by its quality evaluations, thus making tea diversification products evidence based.

## MATERIALS AND METHODS

### Reagents

All chemicals and reagents used were either of analytical or HPLC grade and were purchased from either Sigma (India) or Merck (India).

### Instruments

Electronic balance (Shimadzu BL-220H, Japan); Bulk density apparatus (Indolab VTAP/MATIC-II, India); Standard sieve 30# (Jayant scientific, India); Hot air oven (Chemi Equipments, India); Tablet compression machine (Cadmach, Ahmadabad, India); Friability apparatus (Veego scientific VFT-DV, India); Hardness tester (Monsanto, India); Vernier caliper (Indolab, MITUTOYO, Japan); USP Type I tablet dissolution apparatus (LABINDIA DS 8000); Infrared spectroscopy (Thermo Nicolet Nexus 870)

### Preparation of processed Tulsi- tea extracts (TTE)

Tulsi-tea was prepared by mixing black tea: tulsi in the w/w ratios of 70:30, then filtered, concentrated by rota evaporation, dried and scrapped to get the powdered form that are stored in air tight sterile containers.

### Formulation of TTE loaded solid dosage forms

### Pre formulation studies

Pre formulation studies are done where physical, chemical and mechanical properties of a new drug substance or chemical entities are characterized alone and on combining with excipients in order to develop stable, safe and effective dosage form [7, 8].

### TTE-polymer compatibility studies

Compatibility amongst TTE and the excipients used in the formulations were studied by FTIR analysis. An IR spectrum of TTE and properly blended mixtures of TTE with the excipients were recorded in FTIR spectrophotometer in the scanning range of 500 to 4000 $cm^{-1}$ with a resolution of 4 $cm^{-1}$. The basic purpose was to observe any changes in the spectrum pattern of the TTE due to polymers and thus identify the chances of any chemical interactions.

### Pre compressional studies

The flow properties and compressibility of TTE and excipient powder blends for the purpose of tabletting were evaluated by measuring Angle of Repose (fixed funnel method); Bulk Density (BD) and Tapped Bulk Density (TBD) by Cylinder method; Carr's Compressibility Index using the equation: Carr's Compressibility Index (%) = [(TBD-BD)/ TBD] x100; and Hausner's ratio was determined by the equation**:** Hausner's Ratio = TBD/ LBD**.** Hausner's ratio less than 1.25 indicates good flow while greater than 1.5 indicates poor flow using standard procedures [7, 8]. The values obtained after testing are compared with the standard values and inferences were drawn [Table 2].

## Compression of TTE conventional release tablets

Tulsi tea tablets were prepared by wet granulation[9], the wet dough mass of all well mixed ingredients were passed through sieve no. 16 so as to get uniform sized granules. After 3-4hrs of air drying the granules were further dried in hot air oven for 20-30min at 45˚-50˚C. Dried granules were further sieved and then magnesium stearate and Talc were added as lubricants [Table 1]. Next tablets were subjected to direct compression using single punch tablet machines (Cadmach, Ahmadabad, India). Hardness of the tablets was maintained about 4-5 kg/cm$^2$.

## Quality control

Tulsi tea tablets thus prepared were evaluated for hardness using Monsanto hardness tester; friability was determined using Roche Friabilator; the thickness and diameter of the tablets were determined using Vernier calipers; weight variation test was carried out as per official methods with the specification limit that not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than twice that percentage [10, 11].

## *In vitro* TTE release studies from the formulations

*In vitro* releases of TTE from the tablets have been studied in USP Type I tablet dissolution apparatus (LABINDIA DS 8000) at 37ºC, 100 rpm, and using phosphate buffer media. The rate of release of TTE from the tablets were studied basing on the release of eugenol (marker compound of TTE) analyzed by UV spectrophotometric method [12].

In order to understand the kinetics and mechanism of release of TTE from the formulations, the results of the *in vitro* release studies were fitted to various kinetic equations like zero order (cumulative percent drug release *vs.* time); first order (log cumulative percent drug retained *vs.* time); Higuchi (cumulative percent released *vs.* √time); Peppas (log of cumulative percent drug release *vs.* log time). The kinetic model that best fits the dissolution data were evaluated by comparing the regression coefficient values (r) obtained in various models. The N values (release exponent) in Peppas model were used to characterize different release mechanisms, where values of n=0.5 indicates Fickian diffusion, values between 0.5–1.0 is for non-Fickian diffusion and n=1 indicates zero order [13-18].

## Comparison of dissolution data

The dissolution profiles were further analyzed by difference factor (f1) and similarity factor (f2). Difference factor (f1) is the percentage difference between two curves at each point and is a measurement of the relative error between the two curves. The similarity factor (f2) is a logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent dissolution between the two curves. The following equations were used to calculate f1 and f2 values:

$$f_1=\{[\Sigma_{t=1}n\ |R_t-T_t|]/[\ \Sigma_{t=1}\ ^nR_t]\}\times100$$

$$f2=50\ X\ \log\{[1+(1/n)\ \Sigma_{t=1}^n(R_t-T_t)^2]^{-0.5}\times100\}$$

Where 'n' is the number of points, $R_t$ is the dissolution value of the reference product at time t and $T_t$ is the dissolution value for the test product at time t. For dissolution curves to be considered similar, f1 should be close to zero and f2 should be close to 100. Generally f1 value ranges up to 15 (0–15) and f2 values greater than 50 (50–100) which ensures equivalence between two curves [15, 18].

## Real time stability studies

The main purpose of stability testing is to observe how the quality of a drug substance or drug product varies with time under the influence of temperature, humidity and light and provides recommended storage conditions, re-test periods and shelf-lives. The rate of product degradation at room temperature is time consuming. Thus, accelerated stability studies have been performed. The batch of formulation with most satisfactory *in vitro* TTE release profile and high similarity factor was selected for stability studies. The optimized formulation batch was stored at 40$^o$C, 75% RH in closed high density polyethylene bottles for 1.5 month. The samples were withdrawn after periods of 1 and 2 month and were analyzed for its hardness, TTE content and *in vitro* release [7, 8, 13].

## RESULTS

The compositional details of Tulsi-tea tablets have been presented in Table 1. The precompressional evaluation of the active ingredient an excipients mixed powder blend and the post compressional evaluation after punching the tablets have been provided in Table 2-3. Details of *in vitro* drug release kinetics and stability of the Tulsi tea tablets are given in Table 4-5.

**Table- 1: Formula for conventional release Tulsi tea tablets**

| Ingredient Name | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| TT extract | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |
| Chitosan | 22.5 | 20.6 | 10.5 | 24.5 | 25.5 | 22.5 | 22.5 | 16.8 | 22.5 |
| Lactose | 65.8 | 44 | 12.3 | 14.2 | 0 | 0 | 0 | 0 | 0 |
| Starch | 0 | 0 | 0 | 0 | 0 | 45.6 | 65.5 | 40.8 | 15.8 |
| Talc | 2.5 | 3.5 | 5.5 | 2.5 | 3.5 | 5.5 | 2.5 | 3 | 5.5 |
| Magnesium Stearate | 1.5 | 3.5 | 6 | 1.5 | 3 | 6 | 1.5 | 3 | 5.5 |
| Colloidal Silica/Aerosil | 1.2 | 2.2 | 4 | 1.2 | 3.5 | 6 | 1.2 | 3.5 | 5.5 |
| PVP | 2.5 | 5 | 7.5 | 2.5 | 5 | 7.5 | 2.5 | 5 | 7.5 |

**Table- 2: Pre compressional evaluation of the powder blend**

| Formulation Code | Formulation | Loose Bulk Density (gm/ml)* | Tapped Bulk Density (gm/ml)* | Hausner's ratio * | Carr's index (%)* | Angle of repose (θ°)* |
|---|---|---|---|---|---|---|
| F1 | C | 0.740±0.002 | 0.881±0.001 | 1.182±0.002 | 13.521±0.008 | 24.56±0.695 |
| F2 | C | 0.729±0.003 | 0.879±0.003 | 1.198±0.003 | 15.781±0.003 | 22.96±1.211 |
| F3 | C | 0.702±0.009 | 0.809±0.009 | 1.189±0.002 | 13.928±0.007 | 24.78±0.473 |
| F4 | C | 0.719±0.001 | 0.821±0.003 | 1.151±0.004 | 15.127±0.002 | 23.84±0.512 |
| F5 | C | 0.709±0.004 | 0.874±0.006 | 1.172±0.002 | 14.259±0.005 | 24.95±0.561 |
| F6 | C | 0.782±0.001 | 0.862±0.002 | 1.139±0.004 | 13.964±0.009 | 25.91±0.217 |
| F7 | C | 0.694±0.005 | 0.771±0.005 | 1.136±0.003 | 11.887±0.006 | 25.14±0.712 |
| F8 | C | 0.723±0.001 | 0.862±0.004 | 1.163±0.004 | 14.859±0.004 | 24.85±1.23 |
| F9 | C | 0.673±0.003 | 0.784±0.002 | 1.198±0.004 | 15.367±0.007 | 24.17±0.194 |

*All results have been presented in triplicate in mean±SD values

**Table- 3**: Post compression evaluation of conventional tulsi tea tablets

| Formulation Code | Formulation | Dimension | | Hardness ($kg/cm^2$)* | Friability (%)* | Weight variation (%)* | Drug content (%w/w)* |
|---|---|---|---|---|---|---|---|
| | | Diameter (mm)* | Thickness (mm)* | | | | |
| F1 | C | 7.49±0.002 | 4.62±0.005 | 4.27±0.32 | 0.27±0.04 | 226.74±0.51 | 101.24±0.27 |
| F2 | C | 7.37±0.001 | 4.53±0.002 | 4.31±0.17 | 0.31±0.07 | 226.21±0.98 | 99.12±0.97 |
| F3 | C | 7.67±0.003 | 4.64±0.003 | 4.33±0.21 | 0.29±0.06 | 226.84±0.52 | 100.14±0.87 |
| F4 | C | 7.54±0.006 | 4.61±0.001 | 4.27±0.26 | 0.33±0.02 | 226.16±0.76 | 99.14±0.63 |
| F5 | C | 7.61±0.002 | 4.53±0.002 | 4.24±0.19 | 0.32±0.04 | 226.49±0.64 | 100.51±0.41 |
| F6 | C | 7.67±0.001 | 4.51±0.005 | 4.26±0.21 | 0.31±0.07 | 226.15±0.23 | 100.94±0.36 |
| F7 | C | 7.64±0.005 | 4.53±0.005 | 4.29±0.17 | 0.27±0.06 | 226.57±0.19 | 99.79±0.46 |
| F8 | C | 7.58±0.001 | 4.61±0.003 | 4.32±0.13 | 0.33±0.05 | 226.28±0.37 | 100.13±0.53 |
| F9 | C | 7.60±0.002 | 4.59±0.004 | 4.34±0.37 | 0.32±0.05 | 226.55±0.61 | 99.87±0.64 |

*All results have been presented in triplicate in mean ± SD values

**Table- 4**: Release kinetics from conventional Tulsi tea tablets

| Code | Zero order | | First order | | Higuchi | | Korsemeyer-Peppas | | f2 values |
|---|---|---|---|---|---|---|---|---|---|
| | $R^2$ | $K_0$ ($mg/h^{-1}$) | $R^2$ | $K_1$ ($h^{-1}$) | $R^2$ | $K_H$($mg\ h^{-1/2}$) | $R^2$ | N | |
| F1 | 0.8816 | 4.9643 | 0.8513 | 0.2682 | 0.9712 | 24.316 | 0.9023 | 0.5116 | 80.58 |
| F2 | 0.9647 | 4.0947 | 0.8351 | 0.2963 | 0.9804 | 23.587 | 0.9246 | 0.4994 | 78.98 |
| F3 | 0.9953 | 5.0999 | 0.8057 | 0.2859 | 0.9946 | 24.037 | 0.9846 | 0.5011 | 84.27 |
| F4 | 0.9537 | 4.9171 | 0.8702 | 0.3049 | 0.9761 | 22.535 | 0.8913 | 0.3979 | 77.96 |
| F5 | 0.8889 | 4.8626 | 0.9313 | 0.2451 | 0.9829 | 24.047 | 0.9119 | 0.3151 | 82.16 |
| F6 | 0.9007 | 5.0016 | 0.9016 | 0.2347 | 0.9437 | 23.516 | 0.9371 | 0.5306 | 81.37 |
| F7 | 0.9505 | 4.91049 | 0.8012 | 0.3071 | 0.9784 | 22.674 | 0.9609 | 0.4084 | 82.39 |
| F8 | 0.9414 | 4.8738 | 0.8109 | 0.3113 | 0.9552 | 22.516 | 0.9536 | 0.3536 | 81.34 |
| F9 | 0.9226 | 4.7524 | 0.8841 | 0.2596 | 0.9814 | 24.153 | 0.9439 | 0.4429 | 79.16 |

$K_0$ = zero order rate constant, $K_1$ = first order rate constant, $R^2$ = correlation coefficient, $K_H$= Higuchi constant, N = Koresmeyer Peppas constant, f2 = similarity factor

**Table- 5**: Stability studies of conventional Tulsi tea tablets

| Characteristics | Initial | 1 month | 3 month |
|---|---|---|---|
| Hardness ($kg/cm^2$) | 5.04±0.07 | 5.02±0.01 | 5.00±0.03 |
| TTE content (%mg/tablet) | 99.91±0.02 | 99.87±0.37 | 99.12±0.12 |
| *In-vitro* drug release at 30 min(%w/w) | 94.15±1.23 | 95.174±1.67 | 95.14±1.27 |

All data is expressed as mean ±SD, m = month(s)

## DISCUSSION

As evident from the values of micromeritic studies [Table 2], the tusi tea extract and the excipients powder blend exhibited excellent flow properties. The quality control evaluations of the compressed tulsi tea tablets [Table 3] showed that the batches pass the evaluations. Basing on the values of release kinetics [Table 4], batch F3 is considered to be the optimized batch with zero order release kinetics and anomalous flow behavior; the drug release from the formulations is said to follow erosion mechanism. The formulations were stable enough as evident from the results of stability studies [Table 5].

## CONCLUSION

Value addition in tea has gained the research limelight. Incorporation of tulsi in tea though adds value but in many cases suffers from organoleptic acceptability. Thus development of tulsi tea tablets is a tea diversification product.

## REFERENCES

[1]. Mitra A, Dewanjee D, Dey B. Mechanistic studies of lifestyle interventions in Type 2 diabetes. *World J Diabetes.* 3(12), 2012, 201-207.
[2]. Mitra A. Effects of a Composite of Tulsi Leaves, Amla, Bitter Gourd, Gurmur Leaves, Jamun Fruit and Seed in Type 2 Diabetic Patients. *J Clin Diagn Res*. 6, 2007, 511-520.
[3]. De B, Bhandari K, Singla RK, Katakam P, Samanta T, Kushwaha DK, Gundamaraju R, Mitra A. Chemometrics optimized extraction procedures, phytosynergistic blending and *in vitro* screening of natural enzyme inhibitors amongst leaves of Tulsi, Banyan and Jamun. *Pharmacog Mag.* 11(44), 2015, 522-532.
[4]. Sen G, Bera B. Black tea as a part of daily diet: A boon for healthy living. *IJTS*. 9(2–3), 2013, 51-59.
[5]. Bhandari K, De B, Katakam P, Adiki SK, Mitra A. Development, quality control of CTC black tea solid dosage formulations and *in vivo* evaluations of its AChE inhibitory effects. *IJOPILS*. 5(1), 2016, 9-34.
[6]. Ghosh Hajra N, Yang CWM. Diversification of the Tea Products - Global Scenario. *J Tea Sci Res*. 5(3), 2015, 1-10.
[7]. Radhika PR, Karanam D, Sivakumar T. Fabrication of sustained release matrix tablets of venlafaxine hydrochloride using eudragits. *IJRAP*. 2, 2011, 1386-1389.
[8]. Atul AB, Prashant Z, Chandewar AV, Jaiswal SB. Designing and Evaluation of Extended Release Tablet of Venlafaxine Hydrochloride Using Hydrophobic Matrix. *Pharm Lett*. 2, 2010, 329-335.
[9]. Verma S, Kumar V, Mishra DN. Design and characterization of bacteria friendly natural matrix tablet of zidovudine hydrochloride in colon cancer. *Pharm Lett*. 6 (6), 2014, 232-238.
[10]. Phoke SV, Sakarkar DM, Mitkare SS. Formulation and characterization of sustain release matrix tablets of venlafaxine hydrochloride by using natural polymers. *Int J pharm front*. 2, 2012, 14-26.
[11]. Raju K, Deepika B, Prasanna L, Gouthami M, Anusha G. Formulation and *in vitro* evaluation of nizatidine floating tablets: effect of natural and synthetic polymers on floating properties. *IJAPR*. 4, 2013, 1358–1367.
[12]. Pramod K, Ansari SH, Ali J. UV Spectrophotometric Method for the Quantification of Eugenol during *in vitro* Release Studies. *Asian J.Pharm Ana*. 3(3), 2013, 86-89.
[13]. De B, Bhandari K, Katakam P, Adiki SK, Mitra A. Formulation, quality evaluations, pharmacokinetic studies and development of IVIVC of phytocomposite loaded solid dosage formulations. *IJDDT*. 7(1), 2017, 1-12.
[14]. Demirturk E, Oner L. Evaluation of *in vitro* dissolution profile comparison methods of immediate release Gliclazide tablet formulations. *J Faculty Pharm*. 25, 2005, 1–10.
[15]. Costa P, Lobo MS. Modelling and Comparison of Dissolution Profiles. *Eur J Pharm Sci*. 13, 2001, 123–33.
[16]. Colombo P, Bettini R, Santi P, Peppas NA. Swellable Matrices for Controlled Drug Delivery, Gel Layer Behaviour, Mechanisms and Optimal Performance. *Pharm Sci Technolo Today*. 3, 2000, 1-12.
[17]. Ritger PL, Peppas NA. A Simple Equation for Description of Solute Release II. Fickian and Anomalous Release from swellable Devices. *J Control Release*. 5, 1987, 37-42.
[18]. Ma MC, Lin RP, Liu JP. Statistical evaluations of dissolution similarity. *Stat Sin*. 9, 1999, 1011–1027.