How to Cite:
Gupta, V., & Kori, M. L. (2022). Formulation development and evaluation of novel polyherbal tablet with complete antidiabetic solution. *International Journal of Health Sciences*, *6*(S8), 1189–1197. https://doi.org/10.53730/ijhs.v6nS8.9878

Formulation development and evaluation of novel polyherbal tablet with complete antidiabetic solution

Vikash Gupta
Vedica College of B. Pharmacy, RKDF University, Airport Bypass Road, Gandhi Nagar, Bhopal, 462033, Madhya Pradesh, India

Mohan Lal Kori
Vedica College of B. Pharmacy, RKDF University, Airport Bypass Road, Gandhi Nagar, Bhopal, 462033, Madhya Pradesh, India
Corresponding author email: mohanlalkori@gmail.com

***Abstract*---**Four herbal drugs with the complete antidiabetic solution were selected based on documented properties. Poly-herbal combinations containing 50 % hydro-alcoholic extracts, having the most significant overall antidiabetic activity were selected and polyherbal uncoated tablet (PHUT) was developed. 500 mg PHUT were developed, by homogeneously mixing 250 mg/tablet, dried and finely powdered extracts of four herbs in the most effective ratio, i.e. *H. sabdariffa* (100): *A. marmelos* (50): *F. religiosa* (75): *A. squamosa* (25), with excipients (250 mg/tablet) by direct compression method. For formulation optimization, 3 different formulations were developed by using the same excipients in different ratios and were evaluated for good flow properties and good packing ability. After pre-compression studies, powdered blends were directly compressed and were evaluated using post-compression parameters. Developed PHUTs were dark reddish-brown and devoid of any rough surface. Post compression parameters showed that all parameters are within the limit for all PHUT formulations. Out of all, PHUT 3 showed a significant average disintegration time of 9.40 minutes; hence it was considered as an optimized formulation and was subjected to 3 months accelerated stability studies. Where no significant changes were observed, PHUT 3 was considered a standard formulation with a complete antidiabetic solution.

***Keywords*---**antidiabetic, direct-compression, polyherbal formulation, uncoated tablet.

Introduction

Herbal drugs have been employed for the treatment of different ailments including diabetes, from the time immortal. Even though there are numerous allopathic medications to treat diabetes, however, it is also the reality that it has in no way been reported that someone had completely recovered from diabetes. Apart from that, allopathic treatments are expensive, have clinical complications, and many adverse consequences are also associated (Ganesan *et al.,* 2021; Triplit, 2006). Presently, enormous concerns have been aimed at the management of diabetes by using antidiabetic medicinal plants. Herbal medicines are also employed as complementary therapy for the treatment and prevention of diabetes complications (Patel *et al.,* 2012). Treatment with herbals has several advantages over allopathic drugs, for instance, it has relatively fewer side effects (Karimi *et al.,* 2015; Kooti *et al.,* 2016) and has a rich source of phytochemicals thus can become a substitute for synthetic antidiabetic agents. In search of a complete antidiabetic herbal drug, plants were selected based on their wide coverage, significant therapeutic action, raw material availability, active constituents, mode of action, and minimum toxicity reported. Hence, the polyherbal combinations developed and evaluated will not only control and manage diabetes but will also protect from serious complications associated with diabetes including hyperlipidemia, nephrotoxicity, hepatotoxicity, neurotoxicity, CBC disorder (anemia), and weight reduction (Bagheri, 2008). Based on the above criteria, four plant parts selected were calyx of *Hibiscus sabdariffa,* Linn. (H), leaves of *Aegle marmelos* (L.) Corr. (A), stem bark of *Ficus religiosa* Roxb. (F), and leaves of *Annona squamosa* Linn. (A) *(hereinafter* HAFA). To ensure the safety and efficacy of selected plant parts, their commercially available products were also reviewed; leaf of *Annona squamosa* is available as Sitafal leaf extract drop by Algene biotech and Foodicine. Leaf of *Aegle marmelos* is available as powder by Indianjadibboti.com, and mother tincture by Schwabeindia.com. The bark of *Ficus religiosa, as* Nyagrodhadi Churna by VHCA Ayurveda, Sarivadyasava (Kerala Ayurveda Saribadyasavam, Kottakkal Saribadyasavam), Arjun tea by Planet Ayurveda (Amazon, 2018) and calyx of *Hibiscus sabdariffa,* by Herbal Terra LLC, its Holy Natural Hibiscus Powder (Holy Natural / Nature's gift) and in Herbal Tea (Kashmir) by Sattvic foods.

Polyherbal combinations developed by 50 % hydro-alcoholic extracts of selected plant parts by geometrical dilution method were assessed against diabetes and associated complications and were found to be significantly effective in improving plasma insulin, Homeostasis model assessment-insulin resistance (HOMA-IR), glycosylated hemoglobin (HbA1C), hematological parameters, altered liver, kidney, and neurons function. (Gupta and Kori, 2022). In the present research, it was planned to develop polyherbal uncoated tablets (PHUT), from the most effective HAFA combinations having complete diabetic solutions.

Tablet formulation was selected to develop, because of its economic and ease of manufacturing. Apart from that, it had many advantages over other dosage forms. It offers the utmost dose precision with the least content variability. They are the easiest and cheapest to package and strip. Overall costs are low, are lighter, and are compact (Lachman *et al.,* 1990; Kaur, 2013). Have the greatest chemical and microbial stability over other oral dosage forms. They are suitable for large-scale

production (Ubhe and Gedam, 2020). In the study it was planned to develop standard compressed tablets *i.e.,* uncoated tablets made by direct compression methods, as it provides rapid disintegration and drug release, and exerts local action in the gastrointestinal tract. In addition to medicaments compressed tablets usually contain excipients such as diluents, binders, disintegrants, etc. Thus in the research study, polyherbal uncoated tablet (*hereinafter* PHUT) were prepared by direct compression method and were evaluated using standard parameters at different stages. Table 1 (a) and (b) show standard evaluation reference parameters used for pre-compression study and table 2 shows standard evaluation reference parameters used for the post-compression study.

Materials and Methods

Equipment and excipients used in PHUT development included, **s**ieves number 30, glass and lab wares, tablet compression machine (14 mm round standard convex punch), Vernier caliper, Monsanto hardness tester, Roche friabilator and Electrolab disintegrating apparatus. All chemicals used were of analytical grade like; microcrystalline cellulose 20 – 60 % in PHUT, croscarmellose sodium 3 – 6 %, colloidal silicon dioxide 1 %, and magnesium stearate 1 – 1.5 %.

Extracts used as active ingredients in the formulation of PHUT were prepared by using four plants parts of HAFA, which had a ratio of *H. sabdariffa* (100): *A. marmelos* (50): *F. religiosa* (75): *A. squamosa* (25). Firstly powdered herbal drug was defatted with petroleum ether and then subjected to extraction with a hydroalcoholic solvent containing 50% ethanol v/v using soxhlet. The extracts were concentrated under reduced pressure, dried, and kept moisture-free using desiccators. These dried and finely powdered extracts were used as active ingredients in tablet manufacturing. Before processing, all the dried and finely powdered plant extracts were mixed properly for 10 minutes and were sifted through a 30# sieve to get the uniform mixture.

500 mg PHUT (uncoated tablet) formulation was developed by mixing HAFA extracts with selected excipients. For formulation optimization, three different formulations PHUT 1, 2 and 3, were developed using excipients in different ratios as given in table 3, to get good flow properties and good packing ability (Shah *et al.,* 2008; Patel *et al.,* 2017). It tablet formulation, extracts and excipients was homogeneously mixed for 30 minutes except for colloidal silicon dioxide and magnesium stearate. After mixing the mixture for 30 minutes, colloidal silicon dioxide was added and was blended for the next 5 minutes and at last magnesium stearate was added and blended for 5 minutes. Mixtures were finally subjected to pre-compression studies, before tablet compression. After pre-compression studies, powdered blends were compressed by a tablet compression machine using a 14 mm round standard convex punch for 500 mg strength of tablets. The area were processing was done, its temperature was maintained at 25 ± 2° C and 30 ± 2 % relative humidity was maintained. The direct compression technique that was used to prepare PHUT was selected due to its economic nature and convenience for small-scale preparations (Agnihotri and Singh, 2014).

Before compression of the tablet, pre-compression studies were performed for PHUT 1, 2 and 3 formulations, to ensure uniform flow and compression of the tablet. The evaluation was done by determining bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio as per Indian Pharmacopoeial standards (Iqubal, 2014). Results obtained from the evaluation of powdered blends were studied and were further sent for direct compression of the polyherbal tablets, following standard procedures. (Majumder and Paridhavi, 2016; Mamatha, 2017).

Formulated tablets PHUT 1, 2 and 3 were subjected for post compression studies including physical parameters like general appearance, thickness, hardness, weight variation, friability and disintegration (Patel *et al.,* 2017; Brijyog *et al.,* 2019). In the general appearance study, tablets were examined using the lens under a light for a general appearance like the color, odor and texture. Tablets thicknesses were measured in millimeters using a vernier caliper. A hardness test was performed using calibrated Monsanto hardness tester on ten tablets. In the weight variation test, each tablet was weight individually and the average weight was determined by randomly selecting and weighing 20 tablets. In each case the deviation from the average weight was calculated and expressed as in percentage. The Friability of the tablets was tested as per pharmacopeia by using a Roche friabilator (100 revolutions at 25 rpm). The friability was calculated by using the equation,

$$\text{Per cent friability} = [W0 - Wt / W0] \times 100.$$

Where, W0 = initial weight of tablets, Wt = final weight of the tablets.

A disintegration test was performed by using the electrolab disintegration apparatus. One tablet was placed in each of the six tubes of the basket and the immersion liquid temperature was maintained at 37 ± 0.50° C. Then apparatus was run as per the machine standard operating procedure. The time required for complete disintegration *i.e.,* no particles was left above the gauge and tablet has passed through the 10# mesh screen, was noted.

The selected PHUT formulation was subjected to stability studies. The accelerated stability studies were carried out according to ICH guidelines by storing the samples at 25° C /60% RH (relative humidity), 30° C/60% RH and 40° C /75% RH for 3 months. The polyherbal tablets were assessed for physical changes, tablet thickness, hardness, weight variation, and percent friability and disintegration time. Finally, they were compared with those tablets which were evaluated immediately after manufacturing (Brijyog *et al.,* 2019).

Results and Discussions

500 mg PHUT was prepared by using different excipients and HAFA extracts. The polyherbal formulation (uncoated tablets) was developed with an aim of convenience to take, enhanced pharmacological activity, and faster and safer action (Majumder and Paridhavi, 2016). The 500 mg polyherbal uncoated tablets (PHUT) were developed by using the direct compression method (Mahendra *et al.,* 2018). Three formulations, i.e., PHUT 1, 2, and 3 were developed using different ratios of excipients for formulation optimization and were evaluated.

Three formulations PHUT 1, 2, and 3 containing a specific ratio of excipients with excipients were evaluated on pre-formulation parameters. Powdered blends subjected to pre-compression, revealed that all parameters are within the acceptable limit and hence would have good flow property and compressibility in form of a tablet**.** The data given in table 4 reveals the same. Developed PHUT tablets were further evaluated using standard parameters. (Iqubal, 2014).

The prepared three formulations of uncoated poly herbal tablets were evaluated for different post-compression parameters such as general appearance, thickness, hardness, weight variation, friability, and disintegration time, (summarized in the table. 5 and 6) were results showed that all the parameters were found within the acceptable limit. Table 5 reveals the physical characteristics of the developed PHUT, where it was reported that all the PHUT were of dark reddish-brown and devoid of any rough surface throughout, the surface of all tablets was found to be smooth without imperfections. In evaluation, study friability was found to be less than 1.0 percent. The disintegration time for the tablet was in the range of 9.40 to 11.20 minutes. The formulation PHUT 3 showed a significant average disintegration time of 9.40 minutes, hence PHUT 3 was considered an optimized formulation.

The final formulation PHUT 3 was subjected to an accelerated stability study for any change in physical appearance and other standard parameters at different relative humidity and temperature for 3 months. At one month interval, the samples were analyzed thoroughly for any specified and notable changes. By the study, it was observed that the surface was devoid of any change in color, odor, or appearance of any roughness. Results, as mentioned in table 7, revealed that there were no significant changes in all parameters analyzed and it may be considered that the PHUT formulation developed was a stable formulation.

Conclusion

By the study, it was concluded that developed PHUT formulation number 3 is the standard formulation that can be considered for the complete antidiabetic solution.

Acknowledgement

The authors are greatly thankful to the Research cell, Vedica college of B.Pharmacy, RKDF University, for providing necessary research facilities.

References

Agnihotri, A., Singh, V. (2014). Formulation development and evaluation of antidiabetic polyherbal tablet. The *Pharma Innovation Journal,* 3(6), 01-03.

Bagheri, S.C., & Jo, C. (2008). Clinical review of oral and maxillofacial surgery.*Mosby*. 363-409. https://doi.org/10.1016/B978-0-323-04574-2.50019-3.

Brijyog., Singh, L.P., Kumar, S., and Verma, S. (2019). Anti-diabetic activity of hydroalcoholic extracts of *Anacardium occidentale*, *Aegle marmelos* and

Achyranthes aspera in alloxan-induced diabetic rats. *International Journal of Pharmaceutical Sciences and Research,* 10(11), 4932-4936.

Ganesan, K., Rana, M.B.M., Sultan S. (2021). Oral hypoglycemic medications. In: StatPearls [Internet]. Treasure Island (FL) : StatPearls Publishing; https://www.ncbi.nlm.nih.gov/books/NBK482386/

Gupta, V and Kori, M.L. (2022). Development and assessment of polyherbal formulation for management of diabetes and its associated complications. *Ph.D. Thesis*, RKDF University, Bhopal.

Iqubal, M.K. (2014). Recent advances in direct compression technique for pharmaceutical tablet formulation. *International Journal of Pharmaceutical Research & Development*, 6(01), 049 – 057.

Karimi, A., Majlesi, M., & Rafieian-Kopaei, M. (2015). Herbal versus synthetic drugs; beliefs and facts. *Journal of Nephropharmacology*, 4(1), 27–30.

Kaur, R., Afzal, M., Kazmi, I., Ahamd, I., Ahmed, Z., Ali, B., Ahmad, S., and Anwar, F. (2013). Polypharmacy (herbal and synthetic drug combination)- A novel approach in the treatment of type-2 and its complications in rats. *J Nat Med*, 67,662-671.

Kooti, W., Farokhipour, M., Asadzadeh, Z., Ashtary, L.D. & Asadi-Samani, M. (2016). The role of medicinal plants in the treatment of diabetes: a systematic review. *Electronic physician*, 8(1), 1832–1842. https://doi.org/10.19082/1832.

Lachman, L., Lieberman, H.A., Kanig, J.L. (1990).The theory and practice of industrial pharmacy,*Varghese Publication House*, 3, 293-373.

Mahendra, K.S., Vijay, K.S., Prakash, S.R. (2018). Development and evaluation of antidiabetic potential of polyherbal formulation in streptozotocin induced animal model. *Int J Cell Sci & Mol Boil*, 5(2), 555656. https://doi.org/10.19080/IJCSMB.2018.05.555656.

Majumder, P., and Paridhavi, M. (2016). Physiocochemical standardization and formulation development of poly-herbal tablet for diabetes. *British Journal of Pharmaceutical Research.* 12(3):1-17.

Mamatha, D. (2017). Formulation and evaluation of poly herbal anti-diabetic tablet dosage form. *International Journal of Ayurvedic and Herbal Medicine*, 2956–2962. https://doi.org/10.18535/ijahm/v7i6.06.

Patel, D.K., Kumar, R., Laloo, D., & Hemalatha, S. (2012). Diabetes mellitus: an overview on its pharmacological aspects and reported medicinal plants having antidiabetic activity. *Asian Pacific journal of tropical biomedicine,* 2(5), 411–420. https://doi.org/10.1016/S2221-1691(12)60067-7.

Patel, K., Lal, H., Jain, V. (2017). Formulation, development and evaluation of antidiabetic polyherbal tablet*. International Journal of Pharmaceutical Sciences Review and Research*. 42(2),27,146-151.

Shah, R.B., Tawakkul, M.A., Khan, M.A. (2008). Comparative evaluation of flow for pharmaceutical powders and granules. *AAPS Pharm Sci Tech*, 9,250–258.

Subagiyo, A., Afdhal, A. F., & Derriawan, D. (2020). The influence of product upgrading and quality on customer satisfaction and its impact on consumer loyalty standardized herbal medicine: Research on Tolak Angin Sido Muncul Product in DKI Jakarta. *International Journal of Health & Medical Sciences*, *3*(1), 136-145. https://doi.org/10.31295/ijhms.v3n1.330

Triplitt, C. (2006). Drug interactions of medications commonly used in diabetes. *Diabetes Spectrum.* 19, 4, 202-211.

Ubhe, T., & Gendam. (2020). A brief overview on tablet and its types. *Journal of Advancement in Pharmacology*, 1. 21-31.

Widana, I.K., Sumetri, N.W., Sutapa, I.K., Suryasa, W. (2021). Anthropometric measures for better cardiovascular and musculoskeletal health. *Computer Applications in Engineering Education*, *29*(3), 550–561. https://doi.org/10.1002/cae.22202

Table 1 (A) Pre-Compression Parameters of the Tablets

Type of flow	Angle of repose	Compressibility index	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-30	1.35-1.45
Very poor	56-65	31-35	1.46-1.59
Very, very poor	>66	>35	>1.60

Table 1 (B) Pre-Compression Parameters of the Tablets

S.No.	Standard parameters	Reference value
1.	Bulk density (g/ml)	0.1 – 0.7 (g/ml)
2.	Tapped density (g/ml)	0.1 – 0.7 (g/ml)

Table 2 Post-Compression Parameters of the Tablets

S.No.	Evaluation parameter	Remark
1.	Thickness (mm)	±5% variation of a standard
2.	Weight variation	±5% (I.P.)
3.	Hardness (kg/cm^2)	Not less than 3 (5-8 kg/cm^2)
4.	Thickness (mm)	acceptable limit ±5%
5.	Per cent friability	0.5 - 1% of standard
6.	Disintegration time (minute)	Ideal disintegrate time less than 15 minutes

Table 3 Excipients used in Polyherbal Tablet Formulations

Compositions per tablet	PHUT 1	PHUT F2	PHUT F3
HAFA herbal extracts	250	250	250
Excipients used			
Microcrystalline cellulose	222.5	212.5	202.5
Croscarmellose sodium	15	25	35
Colloidal silicon dioxide	5	5	5
Magnesium stearate	7.5	7.5	7.5
	500	500	500

Table 4 Pre-Compression Studies of Antidiabetic Tablets

Pre-compression parameters	Formulations		
	PHUT 1	PHUT 2	PHUT 3
Angle of repose	27 ^{o}	24 ^{o}	21^o

Bulk density (g/ml)	0.49	0.53	0.49
Tapped density (g/ml)	0.57	0.62	0.54
Carr's index (%)	14.04	14.52	9.26
Hausner's ratio	1.16	1.17	1.11

Table 5 Physical Parameters of the Antidiabetic Tablets

Physical parameters	Formulations		
	PHUT 1	PHUT 2	PHUT 3
Colour	Dark reddish brown	Dark reddish brown	Dark reddish brown
Odour	Characteristic	Characteristic	Characteristic
Texture	Smooth	Smooth	Smooth
Shape	Round standard convex	Round standard convex	Round standard convex

Table 6 Post-Compression Studies of Antidiabetic Tablets

Post-compression parameters	Formulations		
	PHUT 1	PHUT 2	PHUT 3
Average weight (mg)	503.20	502.50	501.10
Weight variation in %	0.64	0.50	0.22
Hardness (kg/cm^2)	5.50	5.52	5.52
Thickness (mm)	4.30	4.28	4.25
Per cent friability	0.24	0.21	0.19
Disintegration time (minute)	11.20	10.50	9.40

Table 7 Accelerated Stability Studies of Antidiabetic Tablets

Parameters	Day 0	30 days			60 days			90 days		
General appearance	Finished Tablets	25° C / 60% RH	30° C / 60% RH	40° C / 75% RH	25° C / 60% RH	30° C / 60% RH	40° C / 75% RH	25° C / 60% RH	30° C / 60% RH	40° C / 75% RH
Colour	Dark reddish brown	NC	NC	NC	NC	NC	NC	NC	NC	NC
Odour	Characteristic	NC	NC	NC	NC	NC	NC	NC	NC	NC
Texture	Smooth	NC	NC	NC	NC	NC	NC	NC	NC	NC
Shape	Round standard convex	NC	NC	NC	NC	NC	NC	NC	NC	NC
Average weight (mg)	501.10 ± 0.3	NC	NC	NC	NC	NC	NC	NC	NC	NC
Weight variation in %	0.22	NC	NC	NC	NC	NC	NC	NC	NC	NC
Hardness (kg/cm^2)	5.52 ± 0.05	5.52 ±	5.52 ±	5.52 ±	5.52 ±	5.52 ±	5.48 ±	5.48 ±	5.45 ±	5.45 ±

Thickness (mm)	4.25 ± 0.10	0.05 NC	0.06 NC	0.06 NC	0.05 NC	0.05 NC	0.04 NC	0.04 NC	0.05 NC	0.05 4.30
% Friability	0.19 ± 0.04	0.19 ± 0.04	0.19 ± 0.05	0.19 ± 0.02	0.19 ± 0.03	0.19 ± 0.02	0.21 ± 0.05	0.21 ± 0.02	0.21 ± 0.05	0.24 ± 0.4
Disintegration time (minute)	9.40 ± 0.30	9.40 ± 0.20	9.40 ± 0.25	9.40 ± 0.10	9.40 ± 0.15	9.40 ± 0.18	9.45 ± 0.12	9.48 ± 0.20	9.50 ± 0.22	9.52 ± 0.14

NC- No change, RH- Relative humidity.