Scholars Academic Journal of Pharmacy (SAJP) **ISSN 2320-4206 (Online)**
Sch. Acad. J. Pharm., 2014; 3(3): 321-326 **ISSN 2347-9531 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Research Article

Development and Evaluation of Polyherbal Tablet from Some Hepatoprotective Herbs

Sanjay Kumar Kushwaha[1], Mohan Lal Kori [2*]
[1]Institute of Pharmaceutical Science and Research Centre, Bhagwant University, Ajmer, (Raj.) – 305004, India
[2]Vedica College of B. Pharmacy, a constituent institute of RKDF University, Bhopal (MP) 462033, India.

***Corresponding author**
Mohan Lal Kori
Email: mlkori.research@gmail.com

Abstract: The objective of the present study was to develop and evaluate hepatoprotective polyherbal tablet because designing of oral herbal formulation is still a challenge in modern pharmaceutics and the tablet formulation presents many technical problems to the industrial pharmacist. Potential hepatoprotective herbs were used for developing polyherbal tablets. Aqueous extract of whole plant of *Momordica dioica*, *Phyllanthus amarus* and *Cassia occidentalis* were used in different concentrations in the formulations. The granules were prepared by a wet granulation technique using isopropyl alcohol. Preformulation study was done to evaluate pre-compression parameters of powder blends. Tablets were prepared by using hand rotating single punch tablet press and were evaluated for post compression parameters, i.e. uniformity of weight, general appearance, hardness, friability, disintegration and *in-vitro* dissolution. Tablets were also subjected for the accelerated stability for the period of three months at accelerated temperature conditions. No marked changes were noticed in all the evaluated parameters during three months of accelerated stability study. The laboratory scale preparation of polyherbal tablet may be used as a stable, solid dosage form and the work done in stability testing may help in the progress of shelf-life determination studies.
Keywords: Hepatoprotective, Polyherbal formulation, Tablet, Stability study.

INTRODUCTION

The present scenario of global market is in urgent need of standardized and reproducible herbal preparations, which can be achieved by the formulation of modern herbal dosage forms and their evaluation by modern techniques. Solid oral dosage forms represent the preferred class of product for orally administered drugs. Advantage beings unit dosage forms, easy to handle and transport, convenient and safe. Considering their convenience, ease of administration and ability to mask unpleasant tastes and odor of herbal extracts, this dosage form was selected. *Momordica dioica* Roxb. (Cucurbitaceae) [1, 2], *Phyllanthus amarus* Schum & Thonn. (Euphorbiaceae) [3, 4], and *Cassia occidentalis* Linn. (Leguminosae) [5] has already been reported for their hepatoprotective activity and is used by some local Ayurvedic practitioners for general liver ailments.

MATERIAL & METHODS

Material

Plant specimens were collected from the herbal garden of Geetanjali Institute of Pharmacy Udaipur (Raj.), India, during the month of August-September 2013. The Voucher specimen H/GIP-927, H/GIP-1027 and H/GIP-1127 were deposited in the Department of Pharmacognosy and received botanic identity and the identity was confirmed by correlating their morphological and microscopical characters. Starch, talc, magnesium stearate and lactose (Loba chemicals Ltd. Mumbai) and other chemicals of analytical grade were used.

Isolation of marker compounds

Fluorescence producing a single component was isolated from aqueous extracts of each drug using preparative thin layer chromatography [6]. The mobile phase n-butanol : acetic acid : water (4:1:5) was found to be the best. The developed plates were dried and subjected to observation and marking under UV light at 365 nm. The fluorescent producing bands were marked and carefully scraped out with the help of spatula from each plate. The scraped material subjected to extraction of fluorescent producing component with methanol from silica gel [7]. The extract was filtered through Whatman filter paper and dried by evaporating at room temperature. The components isolated from *Momordica dioica* was named MD1 (R_f 0.78) whereas the component from *Phyllanthus amarus* was named PA1 (R_f 0.59) and CO1 (R_f 0.89) was named as a marker compound from *Cassia occidentalis*.

Development of formulation

The wet granulation technique was selected due to its convenience for small scale preparations. The standardized extracts and other ingredients in each formula were weighed, ground and screened through sieve number 80 separately. All the ingredients were mixed together except talc and magnesium stearate milled in a pestle mortar and sieved again through sieve number 80. The material was mixed with the acacia gum solution, which was added slowly. After mixing, the powder mass was screened through sieve number 18 to get the granules and dried at 35°C in vacuum dryer. After drying, the granules were again screened through sieve no. 18 to remove bigger granules and stored in desiccators [8].

Preparation of polyherbal tablets:

The tablet granules were prepared by using isopropyl alcohol with different compositions of aqueous extracts of each drug, starch as disintegrator, talc as lubricant, magnesium stearate as glidant, acacia gum as a binder and lactose was used as filler. The formulations were coded as TAB1, TAB2, TAB3, TAB4 and TAB5 (table 1).

Table-1: Formulation of polyherbal tablets

Ingredients	Amount (mg) for one tablet				
	TAB1	**TAB2**	**TAB3**	**TAB4**	**TAB5**
Aqueous extract of *Momordica dioica*	50	25	75	75	25
Aqueous extract of *Phyllanthus amarus*	50	75	25	75	25
Aqueous extract of *Cassia occidentalis*	50	25	75	25	75
Starch	20	20	20	20	20
Talc	5	5	5	5	5
Magnesium stearate	5	5	5	5	5
Acacia gum	5	5	5	5	5
Lactose	315	340	290	290	340

Power blends were compressed to 500 mg tablet on hand rotating single punch tablet presses using 11 X 8 mm punch set with appropriate compression pressure. The granules were mixed with talc and magnesium stearate before punching and the die cavity was adjusted for required weight and the granules were punched to tablets.

Preformulation studies:

The following pre-compression parameters were tested [9, 10].

Angle of repose: Determined by using the funnel method. Accurately weighed granules were taken in a funnel and the height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated from the following formula.

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

Where θ = angle of repose, h = height of powder cone formed, r = radius of powder cone formed

Loose bulk density (LBD): Determined by pouring a weighed quantity of granules into a graduated cylinder and measuring the volume and weight.

LBD = Weight of the powder / volume of the packing

Tapped bulk density (TBD): Determined by placing a graduated cylinder, containing a known mass of granules. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10 cm at two second intervals. The tapping was continued until no further change in volume was noted.

TBD = Weight of the powder / volume of the tapped packing

Hausner ratio: It is the measurement of frictional resistance to the drug. The ideal range should be 1.2-1.5. It is determined by using the following formula:

Hausner ratio= TBD / LBD

Compressibility index: The Compressibility index of the blends was determined by the Carr's compressibility index.

Compressibility index (%) = (TBD-LBD) X 100 / TBD

Loss on drying: One gram of granules was transferred into a dried, glass stoppered shallow weighing bottle. The contents were distributed evenly and placed in the drying chamber. The stopper was removed from the bottle and the contents were dried for a specified time to achieve a constant weight.

Loss on drying (%) = [(Initial weight – Final weight) / (Initial weight)] X 100

Evaluation of Polyherbal Tablets

The following post-compression parameters were employed for evaluation of tablets [11, 12, 13].

Uniformity of Weight: Randomly selected 20 tablets of each formulation were individually weighed.

The average value was calculated and compared to individual tablet weights.

General appearance: While considering the general appearance, the color, odor and texture of the tablet were observed.

Hardness test: Tablet requires a certain amount of strength or hardness and resistance friability to withstand mechanical shocks of handling in all processes. The hardness of randomly selected 20 tablets of each formulation was determined by the Monsanto hardness tester.

Percentage friability test: The friability of tablets was determined by Roche friabilator. Percentage of weight loss of 20 tablets randomly selected from each batch tumbled in friability apparatus. After 4 minutes of rotating at 25 rpm, the dust of tablets was removed and the percentage of weight loss was calculated.

Disintegration test: The disintegration time of tablets was determined using the digital microprocessor based disintegration test apparatus (basket rack assembly, Lab India). One tablet was introduced into each tube and added a disc. The assembly was suspended in a 1000 mL beaker filled in with water. The volume of water was such that the wires mesh at its highest point (at least 25 mm) below the surface of the water, and at its lower point (at least 25 mm) above the bottom of the beaker. The apparatus was operated and maintained at 37±2°C. The time requires to all tablets to disintegrate and pass through wire mesh was noted.

***In vitro* Dissolution test:** This study was carried out using basket type tablet dissolution test apparatus (Lab India). A 900 mL of dissolution medium consists of 0.1 M hydrochloric acid introduced into the vessel of the apparatus and warmed to 37±1°C with a stirring speed of 50 rpm for 2 hrs. Aliquots of 10 mL were withdrawn from a zone midway between the surface of the dissolution medium and top of the rotating blade at predetermined time interval and an equal amount of fresh dissolution media maintained at the same temperature was replaced. The samples were analyzed by measuring the absorbance at 365 nm by UV-visible spectrophotometer (Shimadzu UV-1700). The cumulative percent drug release was calculated using an equation obtained from standard curve.

Accelerated Stability Studies

The stability parameters of a drug dosage form can be influenced by environmental conditions of storage, i.e. temperature, light, air and humidity, as well as the package components. All the formulations were subjected for accelerated stability for the period of 3 months at accelerated temperature conditions, i.e. room temperature (25±2°C)/60% RH, 5°C/Ambient and 40°C/75% RH. The different parameters such as color, odor and the texture of the tablets, average weight, hardness, friability and disintegration time were studied at accelerated temperature conditions [14, 15].

RESULTS AND DISCUSSION

The present investigation was undertaken to design, formulate and evaluate a hepatoprotective polyherbal tablet. The granule was evaluated for angle of repose, characterizes the flow properties and is a characteristic related to interparticulate friction resistance to movement between particles. The granules indicated good flowability with 25-29°. The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of materials because all of these can influence the observed compressibility index. The results of LBD, TBD, Hausner ratio, and compressibility index lies between 22.42±1.24 and 32.95±1.07 % shows good flow properties (table 2).

Table 2 : Preformulation studies of powder blends

Parameters	Powder blends for				
	TAB1	TAB2	TAB3	TAB4	TAB5
Angle of repose	26.1±1.02°	28.4±1.36°	25.6±1.01°	31.2±1.13°	27.3±1.06°
Loose bulk density (g/cm^3)	0.375±0.012	0.398±0.005	0.348±0.015	0.387±0.013	0.393±0.009
Tapped bulk density (g/cm^3)	0.526±0.023	0.513±0.008	0.519±0.016	0.546±0.011	0.578±0.004
Hausner ratio	1.40±0.03	1.30±0.019	1.49±0.014	1.41±0.005	1.47±0.029
Compressibility index (%)	28.71±1.19	22.42±1.24	32.95±1.07	29.12±1.31	32.01±1.08
Loss on drying (%)	0.96±0.007	0.99±0.012	0.980±0.002	0.95±0.019	0.950±0.009

Data represented as mean ± SD, n=3

All tablet formulations were subjected to various evaluation parameters and the results obtained were within the Pharmacopoeia limit. No marked change was observed in the general appearance of the tablets. The test for uniform weight indicates that all the tablets were uniform with low standard deviation values (1.06 to 2.02 %). It was observed that the hardness and friability were remarkably related i.e. tablets presenting lower hardness values also had higher friability values. The hardness of tablets was in a range of 6.5 to 7.2 kg/cm^2 showed appreciable hardness characteristics which facilitated its fast disintegration. The weight loss of tablets in percentage friability was in a range of 0.38 to 0.50 indicated that the tablets are mechanically stable. Disintegration testing is most appropriate when a relationship to dissolution has been established or when disintegration is shown to be more discriminating than dissolution. The time required to disintegrate the tablets was in the range of 11 to 14 minutes and the range was within the pharmacopoeia limit, thus all the formulations passed the disintegration test (table 3).

Table 3: Standardization of formulated hepatoprotective polyherbal tablets

Parameters	Formulations				
	TAB1	**TAB2**	**TAB13**	**TAB4**	**TAB5**
Color	Blackish green	Blackish green	Blackish green	Blackish green	Blackish green
Odor	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Texture	Smooth	Smooth	Smooth	Smooth	Smooth
Weight variation (%)	1.08±0.003	1.06±0.012	2.02±0.008	2.01±0.017	1.81±0.006
Hardness (kg/cm^2)	7.2±0.15	7.0±0.50	6.7±0.76	6.5±0.41	7.1±0.22
Friability (%)	0.47±0.002	0.38±0.013	0.45±0.0034	0.50±0.0026	0.46±0.007
Disintegration time (minutes)	14±1.12	12±1.74	11±1.46	12±1.13	12±1.32

Data represented as mean ± SD, n=3

In vitro dissolution study was carried out with respect to the isolated marker compounds MD1, PA1 and CO1 present in herbal actives. This non specific dissolution was intended to be diagnostic of batch to batch variation. The operative assumption inherent in this procedure was that if the isolated markers are demonstrated to have dissolved within time frame and under specified conditions the tablets do not suffer from formulation related problems. It has been observed that the cumulative percentage of drug release of all the formulations was more than 90 % at the end of 2 hours (figure 1-3).

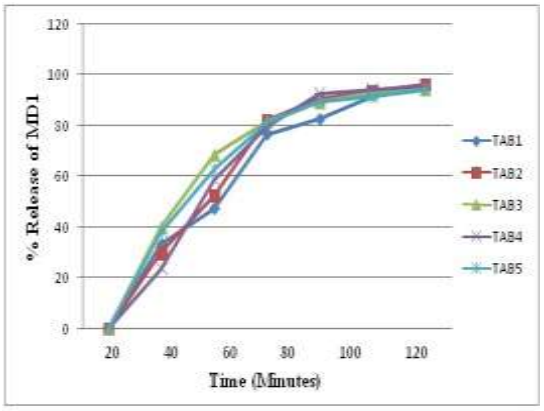

Fig-1: Release profile of compound MD1 of *Momordica dioica.*

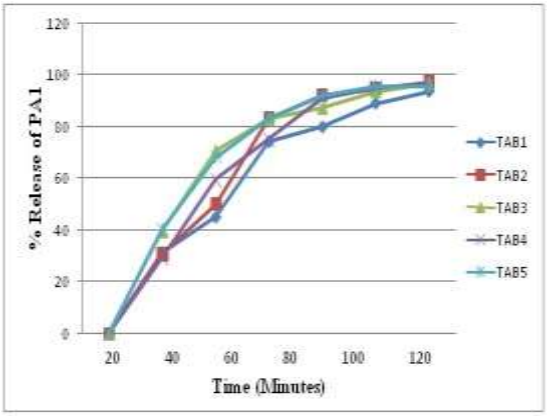

Fig-2: Release profile of compound PA1 of *Phyllanthus amarus*

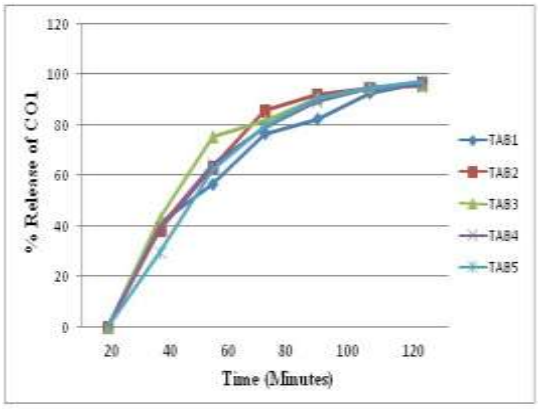

Fig-3: Release profile of compound CO1 of *Cassia occidentalis*

The term stability with respect to herbal dosage form, refer to the chemical and physical integrity of the dosage unit, and when appropriates, the ability of the dosage unit to maintain protection against contamination. No marked changes in color, odor, texture, average weight, hardness, friability and disintegration time were observed in all the formulations (table 4).

Table 4: Accelerated stability studies of tablets

Parameters	Observations									
	Initial	30 days			60 days			90 days		
		RT/ 60%RH	5°C/ Ambient	40°C/ 75%RH	RT/ 60%RH	5°C/ Ambient	40°C/ 75%RH	RT/ 60%RH	5°C/ Ambient	40°C/ 75%RH
Color	Blackish green	NC	NC	NC	NC	NC	NC	NC	NC	Faint green
Odor	Characteristic	NC	NC	NC	NC	NC	NC	NC	NC	NC
Texture	Smooth	NC	NC	NC	NC	NC	NC	NC	NC	NC
Average Weight (%)	1.60	1.60	1.60	1.60	1.60	1.60	1.59	1.59	1.58	1.59
Hardness (kg/cm^2)	6.96	6.96	6.96	6.96	6.96	6.96	6.94	6.96	6.96	6.94
Friability (%)	0.45	0.45	0.45	0.46	0.45	0.45	0.45	0.45	0.45	0.46
Disintegration time (minute)	12.2	12.5	12.3	12.3	12.2	12.4	12.1	12.2	12.2	12.0

NC= No Change, RT= Room temperature (25±2°C)

CONCLUSION

This laboratory scale preparation of polyherbal tablet may be used as a stable, solid dosage form and the work done in stability testing may help in the progress of shelf-life determination. The present study revealed that the composition ratio of ingredients of

polyherbal tablets, not affect the stability parameters. From this study it is concluded that using traditional knowledge and the recent technologies, the medicinal plants can be prepared in the form of cost effective tablet formulations to improve their stability, consumer compliance and acceptability.

ACKNOWLEDGEMENTS

The authors are thankful to Geetanjali University, Udaipur (Raj.) for providing facilities to carry out this work.

REFERENCES

1. Kushawaha SK, Jain Anurekha, Jain Avijeet, Gupta VB, Patel JR, Dubey PK; Hepatoprotective activity of fruits of *Mormordica dioica* Roxb. Plant Archives, 2005; 5(2):613-616.
2. Kushwaha SK, Jain Avijeet, Jain Anurekha, Gupta VB, Patel JR; Hepatoprotective activity of fruits of *Momordica dioica*. Nig J Nat Prod and Med, 2005; 9:27-29.
3. Kushawaha SK, Dashora A, Dashora N, Patel JR, Kori ML; Acute oral toxicity studies of the standardized methanolic extract of *Phyllanthus amarus* Schum & Thonn. J Pharmacy Res, 2013; 6:720-724.
4. Patel JR, Tripathi P, Sharma V, Chauhan NS, Dixit VK; *Phyllanthus amarus*: Ethnomedicinal uses, phytochemistry and pharmacology A review. J Ethnopharmacol, 2011; 138:286-313.
5. Michael AG, Oyeronke AO; In vitro antioxidant/radical scavenging activities and hepatoprotective roles of ethanolic extract of *Cassia occidentalis* leaves in sodium arsenite treated male Wistar rats. British J Med and Medical Res, 2013; 3(4):2141-2156.
6. Agarwal M, Kamal R; Studies on flavonoids production using *in vitro* cultures of *Momordica charanctia* L. Ind J Biotechnol, 2007; 6:277-279.
7. Marston A; Review: Role of advances in chromatographic techniques in phytochemistry. Phytochemistry, 2007; 68:2785–2797.
8. Ghiware NB, Gattani SG, Chalikwar SS; Design, development and evaluation of oral herbal formulations of *Piper nigrum* and *Nyctanthes arbortristis*. Int J Pharm Tech Res, 2010; 2(1):171-176.
9. Aulton ME; Pharmaceutics: The science of Dosage form. Churchill Livingstone, 1996: 304.
10. Lachman L, Lieberman HA, Kanig JL; The theory and practice of industrial pharmacy, 3rd edition. Varghese Publishing House, New Delhi, 1987: 293-639.
11. Anonymous: Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare, Controller of Publication, New Delhi, 2007.
12. Nagasamy VD, Jawahar N, Ganesh GNK, Suresh K R, Senthali V, Samanta MK, Sankar S, Elango K; Development and *in vitro* evaluation of sustained release matrix tablets of theophylline using hydrophilic polymer as release retardant. Int J Pharm Sci and Nanotech, 2009; 2(1):370-375.
13. Sahoo HB, Asati AK, Toppo FA, Kori ML; Evaluation of polyherbal formulation for diuretic activity in albino rats. Asian Pacific J Tropical Disease, 2012; 2(Suppl1):S442-S445.
14. Blume HH, Schug BS; The biopharmaceutical classification system (BCS). Europ J Drug Metabol Pharmacokinet, 1999; 117.
15. Kim Huynh-BA; Handbook of stability testing in pharmaceutical development: Regulations methodologies and best practices. Pharmalytik, Network, Delaware. Springer Science, 2008.