International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Formulate and Evaluate Myrobalan Powder Incorporated Chocolate Drug Delivery System

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Abstract: ***Myrobalan scientifically known as Terminalia chebula is a very popular and one of the important herbal materials employees in traditional system of medicine in India especially Ayurveda. It is reported to have anti - oxidant, anti - microbial, antidiabetic, anticarcinogenic, antiviral, anti - bacteria, antifungal, etc. activities and is recommended to be consumed 1 - 2 g once or twice a day as Ayurveda Pharmacopoeia. The intact fruit is very hard. The powdered pericarp is unpleasant in colour and taste. myrobalan in commercially available as (powder, lozenges, churna) yet there is a continuous need to formulate more reliable delivery methods. In this work myrobalan powder is being tried to be incorporated in chocolate drug delivery system. The present study aims to development and evaluation of myrobalan powder incorporated chocolate drug delivery system. In this work initially pre - formulation studies were carried out which includes particle size analysis, flow properties of powder and phytochemical screening. The formulation of myrobalan incorporated chocolate is prepared by using active ingredient as myrobalan powder and other ingredients such as, cocoa butter, cocoa powder, preservative and sweeting agent. The six different formulation varieties were developed as F1, F2, F3, F4, F5 and F6. The evaluation test was carried out by TLC, Hardness test, Thickness test and stability studies. Myrobalan powder could successfully be incorporated in the chocolate base. White chocolate and dark chocolate were tried F6 was found to be ideal for delivery of myrobalan powder.***

Keywords: Terminalia chebula, Extraction, TLC plate, hardness, thickness, stability chamber, chocolate drug delivery system

1. Introduction

Chocolates are semisolid suspensions of fine solid particles derived from sugar and cocoa (and, depending on the variety, milk), accounting for approximately 70% of the total in a continuous fat phase. The primary chocolate classifications are dark, milk, and white, which range in terms of cocoa solid, milk fat, and cocoa butter concentration.[1]

Chocolate is an anhydrous medium for water - sensitive active compounds that is resistant to microbial growth and hydrolysis. Chocolate is high in saturated fat, polyphenols, sterols, di and triterpenes, aliphatic alcohols, methylxanthines flavones, and antioxidants. Cocoa is the major ingredient of chocolate, and it is high in polyphenols. Medicated chocolate is chocolate that contains enough of the medicine. Salty, sour, bitter, and sweet are the four sorts of taste modalities.[2, 3]

The "flavours" can be detected by combining these ingredients. Children's preferences. The feeling differs greatly from that of adult newborns, and youngsters, in general, prefer sweet - tasting substances. Chocolate has been demonstrated to aid in the production of a chemical known as "Serotonin". Chocolate is one of the most appealing and popular foods among youngsters, so we created a chocolate medicine delivery method.

Chocolate (also known as bittersweet chocolate, semi - sweet chocolate, dark chocolate, or "chocolate fondant") shall contain not less than 35% total cocoa solids, of which not less than 18% shall be cocoa butter, on a dry matter basis contains at least 14% fat - free cocoa solids.[1, 3, 4]

Myrobalan (Terminalia chebula)

Terminalia chebula (T. chebula) is a flowering evergreen tree of the family *Combretaceae*. It has several common names such as black myrobalan, ink tree, or chebulic myrobalan (English), `haritaki (Sanskrit and Bengali), harad (Hindi), harada (Marathi and Gujrati) Karkchettu (Telugu) and Kadukkaya (Tamil). It is well known as 'haritaki' since it carries away all diseases or it is sacred to God Siva (Hara).[3, 4]

Haritaki has several interesting synonyms like 'pathya', since it removes obstructions from the pathways and channels in the body; 'abhaya', since it gives fearlessness; 'amrta', means an ambrosia; 'divya', means a divine herb; 'medhya', means a nerve tonic; 'pranada', means lifesaving; 'jivaniya', means a vitalizing herb; 'vayahstha', means one that promotes longevity and maintains youth; 'rasayana phala', means a rejuvenating fruit etc. In Indian mythology, this plant is supposed to be originated from the drops of ambrosa (Amrita) which fell on the earth when God Indra drunk it. In Tibet, T. chebula is called as the "King of Medicine".[4]

Chemical constituents: Biologically active phytochemical constituents are including chebulic acid, chebulinic acid, ellagic acid, gallic acid, chebulagic acid, tannins, anthraquinone, flavanol, carbohydrates, glucose and sorbitol, it also contains nutrients such as vitamin C, protein, amino acids and minerals.[4, 20]

Medicinal uses: [21]

- These fruits are main ingredient in Ayurvedic medicine.
- The fruit pulp is used for curing and cleansing ulcers and wounds.
- It is used by conjunctivitis patients, for relieving the eyelids.
- Gargling with a decoction made from the fruits is very good for fighting oral ulcers, stomatitis and sore throat.
- Terminalia chebula fruit, mixed with sunth powder and hot water, is used for treating asthma and curing hiccups.

- This fruit is used for fighting many diseases including leprosy, chronic as well as intermittent fever, narcosis, diarrhoea and anorexia.
- It is used for curing nervous irritability and nervous weakness.
- Powdered Haritaki is used along with ghee and honey for curing anaemia.
- A decoction of this fruit is used to fight against hepatitis and obesity

Cocoa Butter: [22]
The mature bean from the Theobroma cocoa plant is used to make cocoa butter (CB) a byproduct of the cocoa bean processing industry. It is a crucial component in chocolate and other confectionery products. Because of its unusual fatty acid makeup, it has special physicochemical features that make it valuable. Very little highly unsaturated fatty acid is present in the main triacylglycerols (TAG) found in CB, which are symmetrical. Palmitic acid, stearic acid, oleic acid, and linoleic acid are its main fatty acids; lauric acid and myristic acid are present in smaller levels.

Cocoa powder: [23]
Cocoa is a source of flavanols, and these phenolic compounds exert beneficial effects on health and aging, and reduce the risk of suffering chronic diseases (cardiovascular diseases, metabolic disorders, cancer). An increasing body of evidence has emerged to suggest that cocoa flavanols potentially are important chemo preventive natural agents. This review summarizes human studies from the past two decades, providing data related to the effects derived from cocoa intake on health and disease. Most human studies have reported beneficial effects of cocoa consumption on health and chronic diseases.

Sweetener: [24, 25]
Sweetening agents are employed formulations designed for oral administration specifically to increase the palatability of the therapeutic agent. Jaggery is a natural sweetener obtained by concentrating the juices obtained sugarcane and/or palm trees. Jaggery can be used as a base for number of sweet dishes in different countries because it has sweet winy fragrance and delicious flavour which lies between brown sugar and molasses. It contains nutrients like protein, vitamins and minerals like iron and copper. It is also used as an energy food having therapeutic advantage so, it can be used for blood purification, regular functioning of liver and keeping blood healthy.

2. Methods

Plant material collection and authentication:
The fruit Terminalia chebula Retz. was collected from Retail store, Bengaluru, Karnataka in the month of september, 2023 and the fruit was authenticated by Dr. Noorunnisa Begum, Curator in the Foundation for Revitalisation of Local Health Traditions (FRLHT), Bengaluru, Karnataka, India.

Milling process: [24, 29]
To mill myrobalan seeds from the fruit, the below steps as be followed:
- Collected the dried myrobalan fruits.
- Broken the dried fruits using mortar.
- Separated the seeds from the dried mesocarp of the fruit.
- Using grinder, the dried mesocarp was crushed into a powder.
- The powder was sieved to remove any coarse particles.
- Stored the milled myrobalan fruit powder in an airtight container.

Extraction:
Fine powder was milled from the fruit material of Terminalia Chebula Retz. was broken using mortar and pestle, the outer covering and the seeds was separated. Then, the outer covering extract - myrobalan mesocarp obtained was sun dried and crushed into fine powder. The milted fine powder was stored in air - tight container, kept in room temperature and used for further study.[25, 29]

Preparation of methanolic extract:
Took 5g of milled myrobalan powder was added to 200ml beaker containing 100ml of methanol and allow it to stand for 48 hours. After 48hours the solution was taken and filtered using filter paper and funnel, the methanolic extract was then collected in another beaker and used for Phytochemical screening test.[30, 34, 35]

Preformulation Studies

Phytochemical screening: [18, 23, 31, 33]
Took 1ml of myrobalan powder extract was taken in test tube and used in various Phytochemical screening as shown in table below

Table 1: Phytochemical screening tests

Test	Observation	Inference
Tannins test	Green colour	Present
Mayer's test	No dull white precipitate	Absent
Hager's test	No yellow precipitate	Absent
Fehling's test	No brick red precipitate	Absent
Lead acetate test	White precipitate	Present
Millon's test	No red colour	Absent
Ninhydrin test	No blue colour	Absent
Dragondraff's test	No orange red precipitate	Absent
Molisch's test	No purple or reddish violet appearance at the junction of liquids	Present

Thin Layer Chromatography test (TLC):
The analytical process of myrobalan methanolic extract, mobile phase was kept ready 6ml ethyl acetate, 2ml formic acid, 2ml of toluene, 1ml of methanol (6: 2: 2: 1) in saturation chamber for 20 minutes. Then a drop of myrobalan methanolic extract sample was dropped on 5x15cm of 2mm thickness silica gel coated TLC plate was used as stationary phase and placed in saturation chamber, allowed the TLC plate in saturation chamber until the solvent reach 3/4th of TLC plate. The TLC plate was taken out and kept in hot air oven for 2 - 3minutes, after that the plate was sprayed the plate with ferric chloride reagent and dry the plate for 10minutes examine in ultra violet light.[7, 15, 33]

Particle size determination:
Taken 500g of myrobalan powder and poured into sieves arranged into sieve shaker apparatus and subjected the apparatus to shake for 20 minutes as shown in figure 4 and

collected the powder retained on each sieve and calculated the weight of retained powder in each sieve.[22, 26]

Melting point method of cocoa butter:
Cocoa butter was kept in porcelain dish and kept on electric water bath and waited until the cocoa butter melted. Melting point of cocoa butter was recorded using thermometer.[19, 25]

Formulation:
6 different types of formulations prepared as F1, F2, F3, F4, F5, F6 which includes 2 batches of normal chocolate F1 - F2, 2 batches of milk chocolate F3 - F4, and 2 batches of dark chocolate was prepared F5 - F6.

Table 2: Formulation

Ingredients	F1	F2	F3	F4	F5	F6
Haritaki	1g	0.5g	1g	0.5g	0.5g	1g
Cocoa butter	8.56g	9.8g	7.56g	7.80g	7.80g	7.8 - g
Cocoa powder	11.50g	10g	7.56g	10g	12g	11g
Icing sugar	7g	8g	8.2g	8g	8g	8g
Milk powder	-	-	3.75g	2g	-	-
Jaggery	-	-	-	-		1g
Total	28.6g	28.3g	28.7g	28.03g	28.3g	28.3g

Preparation:
To a pre heated Petri dish add gm of cocoa butter, slowly gm of cocoa powder, gm of icing sugar and gm of jaggery was added to melted cocoa butter in the Petri dish with continuous stirring to avoid formation of lumps. After preparing the chocolate base at the end myrobalan powder was added.[31, 35]

The medicated chocolate was poured in to silicon mould, left the mould in refrigerator for solidifying.

3. Results and Discussion

3.1 Phytochemical screening of extracts:

A small portion of the Myrobalan powder were subjected to phytochemical test methods to find out the presence of alkaloids, glycosides, flavonoids, phenols, saponins and steroids. To carry out the phytochemical screening, small amount of the Methanolic extract was used.

Table 3: Phytochemical Screening of Extracts Results

Chemical Tests	Myrobalan Extract
ALKALOIDS	
Mayer's reagent	- ve
Hager's reagent	- ve
Wagner's reagent	- ve
Dragondroff's reagent	- ve
GLYCOSIDES	
Baljet test	- ve
Legal test	- ve
PROTEINS	
Millon's test	- ve
Ninhydrin test	- ve
FLAVONOIDS	
Shinoda test	- ve
SAPONINS	
Foam test	- ve
TANNINS	
Ferric chloride test	+ve
Lead acetate test	+ve
CARBOHYDRATES	
Molish's test	+ve
Felhing's test	+ve

Table 4: TLC

Compound	Mobile Phase	Rf Value
Myrobalan	Ethyl Acetate: Formic Acid: Toluene: Methanol (6: 2: 2: 1)	0.71

Particle Size Determination
The average particle size of myrobalan powder and cocoa powder by using sieving method:

Table 5: Particle Size Determination

Sieve No	Trial 1	Trial 2	Trial 3
120	12.54 g	11.28 g	15.03 g
85	35.01 g	31.39 g	31.82 g
60	0.60 g	3.5 g	0.83 g
44	0.04 g	0, 09 g	0.51 g
22	0.20 g	0.26 g	0.10 g
10	0.18 g	0.61 g	0.51 g
Tray	0.30 g	2.39 g	0.73 g
Waste	1.13 g	0.02 g	0.19 g
Total	48.87 g	49.58 g	49.81 g

Calculation:

$$\text{Drug} = \frac{\Sigma \text{ weight size}}{\Sigma \, weight \; of \; powder \; retained}$$

$$\text{Average} = \frac{204.24+209.94+200.07}{3} = 204.75$$

3.2 Melting Point of Cocoa Butter:

Cocoa butter was kept in porcelain dish and placed on electric water bath, waited for melting. Melting point of cocoa butter was recorded by using thermometer. Melting point of cocoa butter is 38°C.

3.3 Flow properties

Angle of repose
20g of Myrobalan powder was taken for angle of repose. To know about the flow properties of the powder.
Formula for angle of repose = $\tan^{-1}(h/r)$

Table 6: Angle of repose data

Parameters	Trial 1	Trial 2	Trial 3
H	3.7 cm	3.6 cm	3.65 cm
R	4.5 cm	4.2 cm	4.35 cm
θ	39.42°	40.36°	39.89°

Bulk Density
We have taken 50g of ***Terminalia chebula Retz*** powder for bulk density. To know about the ratio of mass of an untapped powder and its volume including the contribution of the inter particulate void volume.

Formula to calculate bulk density: Bulk density = mass / volume

Table 7: Bulk density data

Test	Trial 1		Trial 2		Trial 3		Average
Bulk density	Mass	Volume	Mass	Volume	Mass	Volume	0.53 g/ml
	50 g	103 ml	50 g	90.33 ml	50 g	86.33 ml	
	0.485 g/ml		0.553 g/ml		0.579 g/ml		

Tapped Density

We have taken 50g of Myrobalan powder for tapped density. To know about the both flow properties and its compressibility.

Table 8: Tapped density data

Test	**Trial 1**		**Trial 2**		**Trial 3**		**Average**
Tapped density	**Initial**	**Final**	**Initial**	**Final**	**Initial**	**Final**	90.33 ml
	110 ml	90 ml	110 ml	92 ml	110 ml	89 ml	
	90 ml		92 ml		89 ml		

3.4 Evaluation

Appearance:

The physical appearance was visually checked for the texture of the chocolate formulations and the following were the observations:

Colour: Brown

Colour, Order, Shape & Texture:

The presence of any particulate matter in the details was noticed minutely.

Table 9: Physical appearance

Formulations code	Colour	Texture	Shape
F1	Brownies	Smooth	Heart
F2	Brownies	Smooth	Heart
F3	Brownies	Smooth	Heart
F4	Brownies	Smooth	Heart
F5	Brownies	Smooth	Heart
F6	Brownies	Smooth	Heart

Weight

Table 10: Weight variation

Formulation code	Weight
F1	2.85 g
F2	2.82 g
F3	2.86 g
F4	2.82 g
F5	2.82 g
F6	2.83 g

Thickness, Melting point and Hardness

Table 11: Thickness, MP, Hardness data

Formulations code	Thickness (mm)	Melting point (degree Celsius)	Hardness (N)
F1	10	37	11.1
F2	12	32	10.6
F3	09	36	9.5
F4	11	35	10.9
F5	13	34	10
F6	11	39	11.2

3.5 Stability Studies

Stability studies were carried out for the optimized Myrobalan powder incorporated in chocolate; The product was tested from time 0 to time 1 month.

Table 12: Stability studies data

Characteristics	Time 0 day	Time 30 day
Colour	Brown	Dark brown
Melting point	38°C	36°C
Appearance	Smooth	Smooth

4. Summary and Conclusion

- An attempt was made to formulate and evaluate Myrobalan powder incorporated chocolate drug delivery system.
- In this work, an effort was done to develop Myrobalan incorporated chocolate drug delivery system with different chocolate bases like cocoa butter, jaggery, milk powder and cocoa powder.
- Preliminary phytochemical tests and TLC were performed to confirm the major constituents such as tannins, flavonoids, phenols etc.
- Different preformulations studies were conducted to determine the flowability, particle size, melting point and stability of cocoa powder and myrobalan powder and cocoa butter and formulated chocolate.
- The prepared formulations were evaluated for the appearance, texture, solubility, stability, hygroscopicity, pH, viscosity and extrudability.
- Among the formulations, F4 was found to be the optimised formulation based on activity, appearance and characteristics.
- Stability studies showed that Myrobalan incorporated chocolate drug delivery system F6 did not show any significant change in terms of degradation of product, when stored at 40 ± 2 ℃ RH 75± 5 for 30 days
- Therefore, the F6 formulation can be used as a useful candidate for antioxidant, respiratory and digestive activity.

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