FORMULATION AND EVALUATION OF TABLETS USING DRUMSTICK POLYSACCHARIDE AS AN EXCIPIENTS

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A B S T R A C T

The drumstick polysaccharide is obtained from the dried ripped fruits of drumstick i.e. Moringa oleifera (Moringaceae). It is commonly called as shevaga (Marathi) and mongana (Hindi). The polysaccharide from the fruit have been shown to possess many pharmaceutical properties and applications such as suspending agent, surfactant, film former, as a stabilizer, disintegrant. It possesses many cosmetic uses. In the present study the plant material was collected, authenticated and was extracted with appropriate solvent to get the polysaccharide in pure form. The immediate release tablets of metformin were developed and evaluated as a novel dosage form using drumstick polysaccharide as an excipient. The DSC studies have revealed that there were no interaction between the drug and the excipient. The wet granulation method was adopted to prepare the tablets and the best drug release pattern of 99.14 % in 60 min was obtained in immediate release tablet. The drug release pattern was compared with the marketed preparation and it was found that the formulation preparation were comparable with marketed preparations as far as the drug release is concerned.

Keywords: Moringa oleifera, Drumstick Polysacccharide, Metformin , Tablet dosage form

1. Introduction[1,2,3,9]

Recently in the field of pharmaceutical technology great efforts are being directed towards the refabrication of existing drug molecules in a fashion capable of solving problem related to poor water solubility, poor bioavailability, dosing stability toxicity.

Even today, conventional drug delivery system providepromt release of drug but in order to achieve as well as maintain drug concentration. Oral route of drug administration is the most important route for administrating drugs for systemic effects.

Drugs which are orally administered, solid dosage form are preferred because –

- They represent unit dosage form.
- They are cheaper than liquid oral.
- They are not prone to leakage or breakage during transportation.
- Stability is more assured than liquids.
- Less chances of contamination.
- Better suited for large scale production.

Though solid oral dosage forms have number of advantages, have some limitations.

Some of them are-

- Many drugs resist compression.
- Drugs having poor wetting property and slow dissolution rate pose difficulty in formulation of dosage form.

But oral solid dosage form are still popular than any other route of drug administration. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration .It means that drug should be delivered at the predicted rate for specific period of time. Hence the concept of spatial placement (drug targeting) and temporal delivery(rate controlling) arises and thus, controlling or sustaining the drug release can solve the problem. In the form of novel drug delivery system (Ndds),an existing drug

molecule can get a new life , thereby increase its market value,competitiveness and patient life. Among the various NDDS available in market per, oral controlled release system holds the major market share because of their obvious advantage of ease of administration and better patient compliance.

1.1.Conventional release tablet:[19]

Conventional-release tablets are expected to achieve fast tablet disintegration which would dissolve rapidly in the gastrointestinal tract for absorption into the bloodstream. The quality of a tablet affects its disintegration and dissolution in the gastrointestinal tract. Tablet quality is dependent on the physicochemical properties of the active pharmaceutical ingredients (API) and excipients used, as well as the manufacturing conditions employed during tablet compression. The flow properties of granulates have a significant effect on the physical properties and ultimately on the quality of tablets produced. Powder flow from the hopper into the dies of a tableting machine is a direct determinant of tablet weight, hardness and content uniformity of tablets. Powder and granulate flow have been measured using parameters such as bulk or fluff density, tapped density, angle of repose, hausner ratio and Carr's index 2-4 . Various techniques are also available for the measurement of each of these parameters. Some of these techniques, however, suffer from lack of reproducibility and predictability, as a result, no single test is considered as a standard for measurement of powder flow . The quality of compressed tablets is judged by parameters such as uniformity of weight, uniformity of content, drug content, hardness or crushing strength, disintegration time, friability, tensile strength and dissolution time. All these parameters are measured by a series of tests some of which are usually specified in accredited official compendia. A tablet is said to be of good quality if it conforms to all the specifications applicable to that tablet in the official compendia. Other parameters that have been used in tablet quality evaluation are crushing strength-friability ratio (CSFR) and the crushing strength-friability/disintegration time ratio (CSFR/DT). In general, high CSFR values denote strong mechanical strength of tablets while high CSFR/DT values connote tablets of high quality and vice versa.

Ideal Properties Immediate release dosage form:

- It should dissolve or disintegrate in the stomach within a short period In the case of solid dosage.
- Should show first absorption and dissolution of drug.
- Rapid onset of action always seen with immediate release tablets.
- Must be compatible with taste masking.
- Be portable without fragility concern.
- It should not leave minimal or no residue in the mouth after oral administration.
- Provides pleasing mouth feel.
- Exhibit low sensitivity to environmental condition as humidity and temperature.
- Be manufactured using conventional processing and packaging equipment at low cost

Advantages:

- An immediate release pharmaceutical preparation offers-
- Improved stability, bioavailability.
- Decreased disintegration and dissolution times for immediate release oral dosage forms.
- Suitable for controlled, sustained release actives.
- High drug loading is possible.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and amenable to existing processing and packaging machinery.
- Cost- effective.
- Improved compliance added convenience
- Frequent dosing is necessary for drug with short half-life.
- Drug release at a time may produce high plasma concentration which may produce toxicity.

Criteria for Drug Selection:

Poor solubility of the drug and need immediate drug action in case of immediate release dosage form. The immediate release compositions comprise micronized drug in an amount

sufficient to provide the desired daily dosage, that is, an amount of about 10 mg to about 1000 mg, more preferably an amount of about 20 mg to 400 mg.

Immediate release compositions from which about 50% of the micronized drug is dissolved in vitro within about 15 minutes, more preferably at least about 80% of the drug is dissolved in vitro within about 30 minutes . Carrier materials for immediate release compositions preferably are selected to provide a disintegration time less than about 30 minutes, preferably about 20 minutes or less, more preferably about 18 minutes or less.

1.2.Pharmaceutical excipients for solid dosage form[26]

Excipient:

- Pharmacologically inactive ingredient which is added to a pharmaceutical compound
- In many cases, an "active" substance (such as acetylsalicylic acid) may not be easily administered and absorbed by the human body; in such cases the API may be dissolved into or mixed with an excipient.

Requirements of excipients:

- Pharmacologically inert.
- Stable for handling.
- Cost effective.
- No interaction with the drug and other Components.
- No taste, odour and colour.

Note that some people may be allergic to some excipients

-for example, many people are lactose-intolerant.

Functions of excipients:

- For providing essential manufacturing technology functions (binders, glidants, lubricants may be added),
- For enhancing patient acceptance (flavours, colorants may be added),
- For providing aid in product identification (colorants may be added),
- For optimizing or modifying drug release (disintegrants, hydrophilic polymers, wetting agents, biodegradable polymers may be added),
- For enhancing stability (antioxidant, UV absorbers may be added)

Types of excipients:

- Fillers
- Diluents
- Antiadherents
- Binders
- Coatings
- Flavours
- Colours
- Lubricants
- Glidants
- Preservatives
- Sorbents
- Sweeteners

Filler/diluents:

Use: to make required bulk of the tablet .to provide better tablet properties such as to improvecohesion, to permit use of direct compression manufacturing to improve flowability.

Most common fillers in tablets:

- Lactose, sucrose, mannitol.
- Dicalcium phosphate dihydrate.
- Starch.
- Cellulose/microcrystalline cellulose.
- Frequently used, water soluble, improves tablet disintegration. Sucrose-stick to tableting tools Mannit-injection, infusion.
- Good flowability, especially indirect compression.
- In higher amount-decrease the mechanical strength of tablet absorbs the moisture-moisture sensitive APIs decrease the microbiological stability.
- Polysaccharide, can increase the disintegration absorbs the moisture from the air.

Disintegrants:

Disintegrants are substances or mixture of substances added to the drug formulations, which facilitate dispersion of tablets into smaller particles for quick dissolution when it comes in contact with water in the GIT. Ideal properties of disintigrants:

- Good hydration capacity,
- Poor solubility,
- Poor gel formation capacity.

Commonly Used Disintegrants:

- Starch:
  - concentration up to 5-20% of tablet weight
  - swells in contact with water
- Superdisintegrants (e.g. sodium starch glycolate, crosspovidone-cross linked povidone) Swells up to ten fold within 30 seconds when contact water.
- Polyvinyl-pyrrolidone
- Carboxymethyl-cellulose

Binders and adhesives:

Role: Ensure that granules and tablets can be formed with the required mechanical strength (glue that holds powders together to form granules).

- In dry powder form
- In solution

Examples:

- starch paste 5-25%
- gelatine solution 10-20%,
- gum acacia, tragacantha, 10-25%
- glucose syrup 50%,
- cellulose derivative
- polyvinylpyrrolidone 2% (PVP), PEG

Lubricants:

Role: Lubricants

- prevent adherence of granule/powder to die wall and
- promote ejection from the die after compaction,
- reduce inter particle friction and
- improve the rate of flow of the tablet granulation

Disadvantages of lubricants:

Lubricants tend to be hydrophobic, so their levels (typically 0.3 – 2%) need to be optimized:

- Under-lubricated blends tend to flow poorly and show compression sticking problems
- Over-lubricated blends can adversely affect tablet hardness and dissolution rate, as well as tablet strength.

Commonly used Lubricants:

A. Water- insoluble **(**Fatty acids-based) lubricant

- Magnesium Stearate
- Calcium Stearate
- Stearic Acid, stearic acid salt
- Talc
- Silica derivative- colloidal silica such as Cab-O-Sil, Aerosil in 0.25-3% conc.
- liquid paraffin, propylene glycol (PG)

B. water-soluble lubricant

- PEG 6000; less effective
- Magnesium/sodium lauryl sulfate; good lubrication and surface wetting effect

Glidants:

Role: Improve flowability of the powder. They are added during direct compaction and to granulation before tableting (they reduce inter particulate friction). Common Glidants:

- Talc (concentration 1-2 %).
- Colloidal silica (0.2 %).
- Corn Starch 5-10%

Adsorbents:

Adsorbents are the agents that can retain large quantities of liquids. Therefore liquids (Vitamin E, essential oils, eutectics, hygroscopic agents) can be incorporated into tablets by addition of adsorbents. Large surface-adsorbs the moisture Water-absorption capacity: 44-99%Generally the liquid to be adsorbed is first mixed with the adsorbent prior to incorporation into the formulation.

Most commonly used adsorbents:

- anhydrous calcium phosphate,
- starch,
- silica colloidal anhydrous (Aerosil)

Flavours:

Use: give the tablet a more pleasant taste or to mask an unpleasant one. (Chewable tablet)

- Flavouring agents are often thermolabile and so cannot be added prior to an operation involving heat.
- They are often mixed with the granules as an alcohol solution. Ex: citric acid, glycerol, orange oil, menthol, vanillin etc.

Colorants:
Uses: It is added to tablets to

- aid identification,
- improve patient compliance.
- mask of off color drug
- production of more elegant product.

All colouring agents must be approved and certified by FDA. These dyes are applied as solution in the granulating agent.

Example:

- Yellow 6- FD & C sunset yellow
- yellow 5- FD & C Tartrazine
- green 3- FD & C Fast Green
- blue 1- FD & C Brilliant Blue
- blue 2 – FD & C Indigotine
- red 3- FD & C Erythrosine FD & C
- red 22 – FD & C Eosin Y

Sweetners:
They are used in chewable tablet to exclude or limit the use of sugar in the tablets.
Most commonly
used sweetenrs**:**

- Mannitol, lactose, sucrose, Dextrose 72% as sweet as sucrose.
- Saccharin, 500 times sweeter than sucrose. Disadvantage**:** has a bitter after taste
- Aspartame**,** largely replace saccharin., 180 times sweeter than sucrose
- **Disadvantage:** lack of stability in the presence of moisture.

1.3.Tablet Processing:[8]
Pharmaceutical products are processed all over the world using the direct compressing, wet granulation, or dry granulation methods. Method chosen depends on the ingredients' individual characteristics like flow property, compressibility etc. Right choice of method requires thorough investigation of each proposed ingredient in the formula for comprehensive approach for interactions and stability.

Direct compression:
The tablets are made by directly compressing the powdered materials without modifying the physical nature of the materials itself. Direct compression is generally done for the crystalline materials having good physical properties such as flow property, compressibility etc. Main advantages of direct compression are time saving, safety of operations and low cost.

Wet granulation:
This is the most widely used method of tablet preparation. In this method the powders are bound by suitable binder by "adhesion". The binder is added by diluting with suitable solvent prior to addition to the blended powders to form wet granules which in turn are dried suitably to expel the solvent forming dried granules. The surface tension forces and capillary pressure are primarily responsible for initial granules formation. The main advantage being it meets all the requirements for tablet formation though it is multistage, time consuming.

Dry granulation:
The dry granulation process is used to form granules without using a liquid solution. This type of process is recommended for products, which are sensitive to moister and heat. Forming granules without moisture requires compacting and densifying the powders. Dry granulation can be done on a tablet press using slugging tooling. On large-scale roller compactorcommonly referred to as a chilsonator. The compacted mass is called slugs and the process is known as slugging. The slugs are then screened or milled to produce a granular form of tablet materials, which have the good flow properties then original powder mixture. The main advantage of dry granulation is it requires less equipment and eliminates the addition of moisture and the application of heat, as found in wet massing and drying steps of the wet granulation method. The manufacture of oral solid dosage forms such as tablets is a complex multi-stage process under which the starting materials change their physical characteristics a number of times before the final dosage form is produced. Traditionally, tablets have been made by granulation, a process that imparts two primary requisites to formulate compactibility and fluidity. Both wet granulation and dry granulation (slugging and roll compaction) are used. Regardless of weather

tablets are made by direct compression or granulation, the first step, milling and mixing, is the same; subsequent step differ. Numerous unit processes are involved in making tablets, including particle size reduction and sizing, blending, granulation, drying, compaction, and (frequently) coating. Various factors associated with these processes can seriously affect content uniformity, bioavailability, or stability.

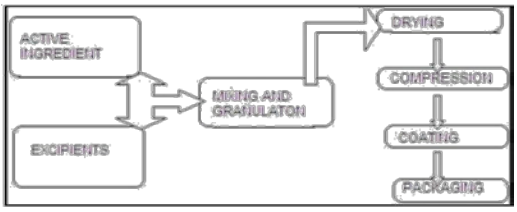

Figure.1 Various Unit Operation Sequences In TabletManufacturing.

Table 1 . Typical Unit Operation Involved In Wet Granulation, Dry Granulation And Direct Compression

Wet granulation	Dry granulation	Direct compression
1. Milling of mixture of drug and excipients 2. Preparation of binder solution 3. Wet massing by addition of binder solution or granulating solvent 4. Screening of wet mass 5. Drying of wet granules 6. Screening of dry granules 7. Blending with lubricant and disintegrant to produce "running powder" 8. Compression of tablet	1. Milling and mixing of drug and excipients 2. Compression into slugs or roll compression 3. Milling and screening of slug and compacted powder 4. Mixing with lubricant and disintegrants 5. Compression of tablet	1. Milling and mixing of drug and excipients 2. Compression of tablet

2. Drug profile -[24]

Drug: Metformine hydrochloride
Description :white powder ,ordourless
Tarde name: glucophage, glumet
Chemical name: 1,1-Dimethylbiguanide hydrochloride
Molecular formula: C4H11N5
Molecular weight: 165.625 g/mol
FDA drug class: Antidiabetic agent
Solubility: freely soluble in water.

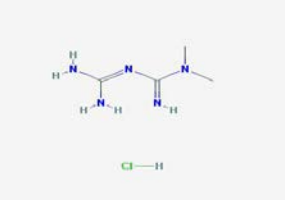

Figure 2: structure of metformin HCl

2.1.Pharmacology:

Two biguanideantidiabetics, phenformin and metformin were introduced in the 1950s. Because of higher risk of lactic acidosis,

phenformin was withdrawn in many countries and has been banned in india 2003.
They differ markedly from sulfonylureas : cause little or no hypoglycaemia in nondiabeticsubjects, and even in diabetics of hypoglycaemia due to metformin are rare. They do not stimulate pancreatic β cells. metformin is reported to improve lipid profile as well as in type 2 Diabetics.
Metformin, an antidiabeticbiguanide, apparently primarily owes its antihyperglycemic action to an effect on the glucose transport through the cell membrane. It thus increases the glucose uptake in the muscle and fat cells. In addition to this, inhibition of the intestinal glucose absorption and of the hepatic gluconeogenesis probably plays a role. Metformin has no influence on the secretion of insulin; however, its effect seems to be dependent on the circulation of small amounts of insulin in the blood. Metformin also has lipid-lowering and hypotensive effectsand it can inhibit the platelet aggregation.

2.2.Pharmacokinetics:
Metformin is not metabolized. It is cleared from the body by tubular secretion and excreted unchanged in the urine; metformin is undetectable in blood plasma within 24 hours of a single oral dose. The average elimination half-life in plasma is 6.2 hours.

2.3.Mechanism of action:

- suppress hepatic gluconeogenesis and glucose output from liver:the major action.
- Enhance insulin-mediated glucose disposal in muscle and fat. Though they do not alter translocation of GLUT4 (the major glucose transporter in skeletal muscle) they enhance GLUT1 transport from intracellular site to plasma membrane. The effects thus differ from that of insulin.
- Retard intestinal absorption of glucose other hexoses, amino acid and vitamin B12
- Interfere with mitochondrial respiratory chain- promote peripheral glucose utilization by enhancing anaerobic glycolysis. However, metformin binds less avidly to mitochondrial membrane.

2.4.Toxicity:
Minor enzyme elevations have been reported to occur during metformin therapy in less than 1% of patients. Indeed, metformin may actually lower elevated aminotransferase levels in patients with fatty liver disease. Clinically apparent liver injury from metformin is very rare, fewer than a dozen cases having been described in the literature despite widespread use of this agent for several decades. The liver injury usually appears after 1 to 8 weeks, typically with symptoms of weakness and fatigue followed by jaundice. Various combinations of hepatocellular and cholestatic injury have been described, and many have been mixed. Allergic manifestations are not typical but rash, fever and eosinophilia have been described. Autoantibody formation is also not typical. Because this agent is usually given in combination with other hypoglycemic agents, many of which also cause liver injury, it can be difficult to establish whether the injury is due to metformin or another agent. The timing of injury is perhaps most characteristic, the injury arising soon after the agent is started and not during long term therapy. Recovery is usually rapid after metformin is stopped.

3. Excipient :[4,5,6,7,10,11,20]
Name : Drumstick
Latin Names:
MoringapterygospermaGaertn./ Moringa oleifera (Moringaceae)

Figure 3: *Moringa oleifera*

Habitat:
It grows wild in the sub-Himalayan tract, from Chenab eastwards to Sarda and is cultivated all over the plains of India.

Morphology Description (Habit):
*M.pterygosperma*is a small or medium-sized tree. The bark is thick,soft, corky and deeply fissured; the leaves, usually tri-pinnate; the leaflets, elliptic; the flowers, white, fragrant in large panicles; the pods, pendulous, greenish, triangular and ribbed with trigonous, winged seeds.

Principal Constituents:
The roots contain an active antibiotic principle, pterygospermin. The root bark contains two alkaloids (total alkaloids, 0.1%), viz. moringine which is identical with benzylamine and moringinine belonging to the sympathomimetic group of bases. It also contains traces of an essential oil with a pungent smell, phytosterol, waxes and resins. An alkaloid, named spirochin, has been isolated from the roots. Hypotensive principles niazininA, niazinin B, niazimicin, and niaziminin A and B were obtained from ethanolic extracts of the fresh leaves. These compounds are mustard-oil glycosides and are very rare in nature.They are rare examples of naturally occurring thiocarbamates

Excipient:[13,18]
Nowdays Most of Researchers are trying to introduce new excipients for drug formulations to exhibit varied functions. The popularity of new excipient research is growing tremendously over the last few decades due to increasing demand for safe, economical and functionally reliable substitutes for the existing synthetic ones. There is almost all therapeutic formulations used for humans and others include excipients. Pharmaceutical excipients can be regarded as totally inert or inactive substance within the formulation, but are used to convert Active Pharmaceutical Ingredients into dosage forms suitable for administration to patient.

Moringa oleifera Lam belongs to family *Moringaceae.* It is also known as Drumstick inEnglish, Saragvo in Gujarati, Soanj-na in Hindi, Sajna in Bengali, Nugge in Kannada, Sigru in Malyalam, Shevga in Marathi, Shobhanjana in Sanskrit and Munaga in Telugu. Moringa powder is sparingly soluble in water but swells in contact with water giving a highly viscous solution. In view of the easy availability of the plant, the ex-udates from the stem of the tree. The stem of the tree exudes a gum which is initially white in colour but changes to reddish brown to brownish black on exposure.

Moringa Oleifera Lam. (*Moringaceae*) is one of the 14 species of the family*moringaceae*,native to India, Africa, Arabia, Southeast Asia, South America, and the Pacific and Caribbean Islands. Because *M. Oleifera* has been seen in many tropic and sub-tropic regions worldwide. The plant is referred to by a number of names such as horseradish tree, drumstick tree, ben oil tree, miracle tree, and “Mother’s BestFriend”. This plant grown and widely cultivated in the northern part of Nigeria and many countries in tropical Africa.*Moringa oleifera* can be grown in a variety of soil conditions preferring well-drained sandy or loamy soil that is slightly alkaline. Almost every part of *M. Oleifera* can be used for food and as a forage for livestock.

Moringa tree was introduced to Africa from India at the turn of the twentieth century where itwas to be used as a health supplement. It is traditionally used for the treatment of a number of ailments including as fomentation to relieve spasm, diarrhea, as diuretic and stimulant in paralytic affliction, epilepsy ad hysteria. Study shows that, for centuries people in many countries have used Moringa leaves as traditional medicine for common ailments.

4. Pharmaceutical application:
Suspending agent:
A comparative study of gums of *Moringaoleifera* and tracaganth was reported. Zinc oxide suspensions were prepared with gum of *Moringaoleifera* and tracaganth. Their sedimentation profile, redispersibility, degree of flocculation and rheological behaviour were compared. The results shows that the suspending properties of *Moringa oleifera gum* are comparable with that of gum tragacanth.

Surfactant behaviour:

A study on interfacial properties and fluorescence of a coagulating protein extracted from *Moringa* seeds and its interaction with sodium dodecyl sulphate (SDS) was carried out. Thestudy reported that

- The protein extracted from Moring seeds has significant surfactant behaviour.
- The coagulant protein interacts strongly with SDS and the protein might have specific binding sites for SDS.
- There is formation of protein-SDS complex.

Film forming property:

Studies reported that gum of *M. Oleifera* has enormous potential for use in the preparation of polymeric films as drug delivery systems.

As stabilizer:

Plant phenolics have gained considerable interest in recent years for their potential effects against food related microorganisms. Phenolic extract obtained from the leaves of *M. oleifera* and *M. orusindica* showed stabilizing activity. In the present study effect of addition of phenolic extract from leaves of *M. Oleifera* and *M. Indica* on the shelf life of pineapple juice stored at 40 °C was investigated by monitoring the changes in titrableacidity and sensory parameters for 8 w. Results observed that the extracts of natural phenolics can be used to improve the quality and safety of foods.

Cosmetic use:

Various parts of *Moringa oleifera* have cosmetic value. Cognis Laboratories Serobiologics team developed Puricare TM and Purisoft TM, two active ingredients based on botanical peptides from the seeds of *Moringa oleifera* tree that purify hair and skin and offer protection against the effects of pollution. *Moringa* seed oil, known as Behen oil is widely used as a carrier oil in cosmetic preparations. The healing properties of *Moringa* oil were documented by ancient cultures. *Moringa* oil possesses exceptional oxidative stability which may explain why the Egyptians placed vases of *Moringa* oil in their tombs. It is high in oleic acid and similar in composition to olive oil. *Moringa* oil is light and spreads easily on the skin. It is good oil for use in massage and aromatherapy applications. It can be used in body and hair care as a moisturizer and skin conditioner. Other uses include soap making and for use in cosmetic preparations such as lip balm and creams. *Moringa oleifera* butter, a semisolid fraction of *Moringa* oil, is used in baby products to contribute a free radical resistant emollient with exceptionally long lasting skin soften.

Binder:[15]

In view of importance of binders in pharmaceuticals for the manufacture of tablets and capsules, gum extracted from the bark of *Moringa Oleifera gum* was evaluate its binding properties through assessment of various parameters essential for pharmaceutical formulation.

Starch:

Starch is also one of the most widely used biomaterial in the food, textile, cosmetics, plastics, adhesives, paper and pharmaceutical industries. The diverse industrial usage of starch is based on its availability at low cost, high calorific value and inherent excellent physicochemical properties. The versatility of starch in industrial applications is clearly defined by its physicochemical properties; therefore, a thorough evaluation of the necessary parameters is important in elucidating its industrial uses. Moringa Oleifera starch as a new starch feedstock for industrial use which can reduce the burden on other starch sources such as cassava, corn, yam, potatoes and other complex carbohydrates. And also to provide an inherent nutritional benefits for various industrial products that use starch as one of the raw material.

Disintegrant:

*Moringaaleifera*isolated gum powder can be effectively used as disintegrant. The disintegration timefor natural gum was found to be less when compared to synthetic gum tablet. All other materials and reagents were of analytical grade of purity.

5. Experimental

5.1. Materials

Metformin was kindly supplied by Medley Pharmaceuticals Lit, Surat, PVP K30, MCC, Lactose, Talc, Magnesium Stearate, Starch, Sulphuric acid, Methanol, Industrial solvent, Acetone was provided by Himedia Lab Pvt Ltd

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5.2. Methodology

Mucilage obtained:

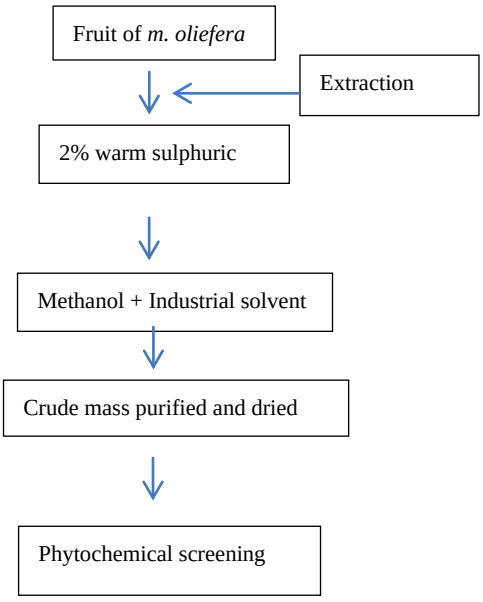

Figure 4: Mucilage of drumstick

Table2: Phyatochemical screening of drumstick polysacharide

Test	Identification test	Observation
Test for carbohydrate		Positive
Test for protein		Negative
Test for alkaloid		Negative
Test for mucilage		Positive
Test for starch		Negative
Test for flavonoids		Negative
Test for glycosides		Negative
Test for tannins		Negative

Table3: Tablet formulation containing different concentrations of excipients

Sr.no	Ingredient	B1 (mg)	B2 (mg)	B3 (mg)	B4 (mg)
1	Metformin	200mg	200mg	250mg	500mg
2	Drum stick powder	15	15	-	-
3	Drumstick	-	-	20	20

	polysaccharide				
4	**pvp k30**	**-**	**-**	**15**	**10**
5	**Starch**	**-**	**-**	**20**	**-**
6	**Mcc**	**25**	**25**	**-**	**-**
7	**Magnesium Sterate**	**5**	**5**	**5**	**5**
8	**Talc**	**5**	**5**	**5**	**5**
9	**Lactose**	**75**	**75**	**80**	**200**

5.3. Results:

DSC Results-

The DSC studies have revealed that there were no interaction between the Drug and the excipients.

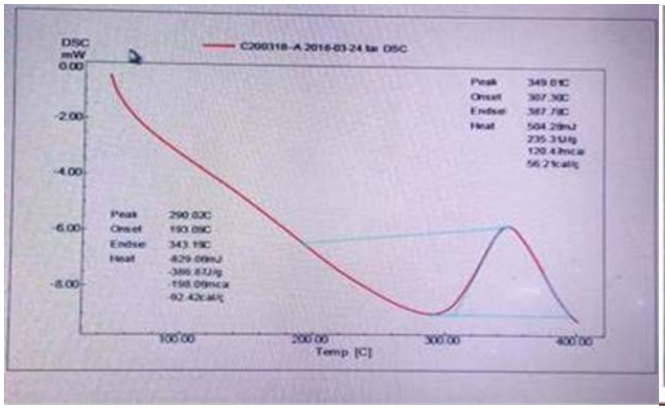

Figure 5: DSC of Sample A

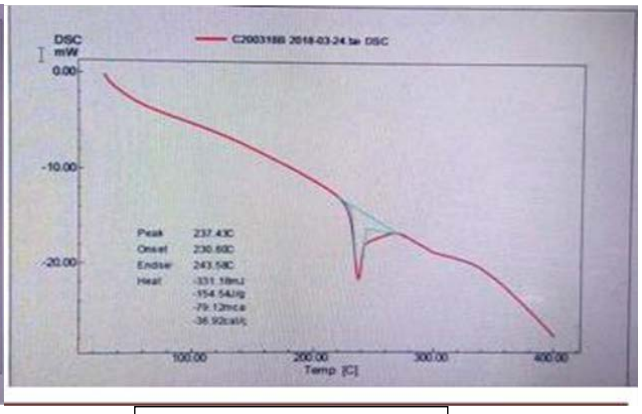

Figure 6: DSC of Sample B

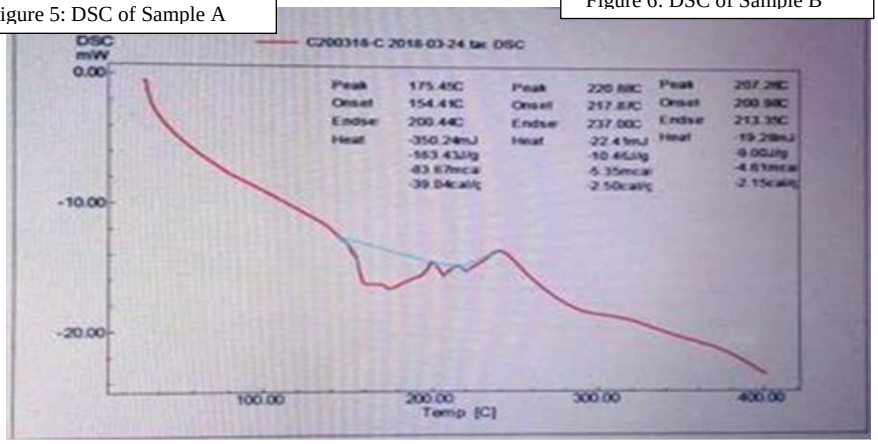

Figure 7: DSC of Sample C

Calibration curve method:

100mg of drug was taken and dissolve in 100ml water 10 ml solution is pipette out in 100ml volumetric flask and volume was make up with water dilution were made from 1ml to 6ml and absorbance was taken at 233nm.

Table.4:Calibration curve of metformin:

Sr no	Concentration (µg/ml)	Absorbance
1	10	0.102
2	20	0.391
3	30	0.732
4	40	1.021
5	50	1.352
6	60	1.658

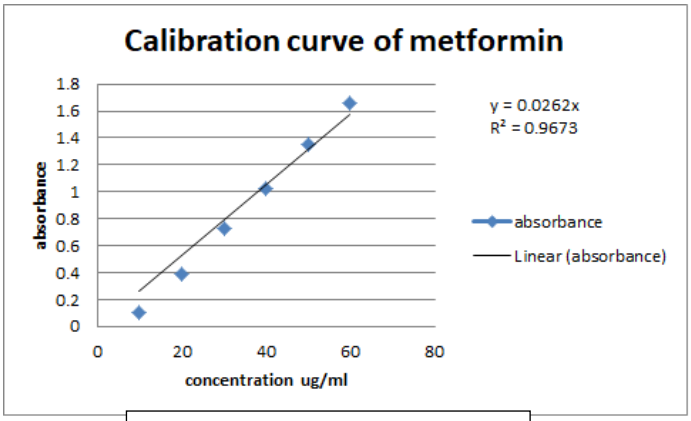

Figure 8: calibration curve of metformin

5.4. Precompression studies results:

Evaluation of granules:

B1-by direct compression, B2 by wet granulation (fast disintrating).

B3 –wet granulation for 250 mg tablet, B4 wet granulation for 500 mg tablet(sustain release)

Table:5: Evaluation of granules

	Bulk density	Tapped density	Carr's index	Hausner's Ratio	Angle of Ratio
B1	0.694	0.883	9.89	1.27	25.96
B2	0.612	0.701	12.85	1.14	27.67
B3	0.653	0.792	17.34	1.21	31.67
B4	0.696	0.828	16.82	1.20	26.05

5.5. Post compression studies results:

Table:6: Evaluation of granules

	Disintegration Time	Thickness (mm)	Diameter	Weight variation	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
B1	20-28sec	0.4mm	0.52mm	325±2	3-4	0.78	99.04
B2	50sec	0.4mm	0.52mm	325±4	3-4	0.65	98.93
B3	-	0.4mm	0.54mm	395±4	4-5	0.51	98.60
B4	-	0.5mm	1.2mm	745±5	5-6	0.29	94.82

5.6. Dissolution studies:

Table 7: dissolution studies of Immediate release tablet

Time(min)	%CR of 200 mg directly compressed Method	%CR of 200mg wet granulation method	%CR of marketed Preparation
10	37.35	78.79	53.45
20	48.49	85.25	66.89
30	49.04	89.60	69.28
40	51.52	91.34	71.87
50	53.02	94.44	74.05
60	54.03	99.18	78.44

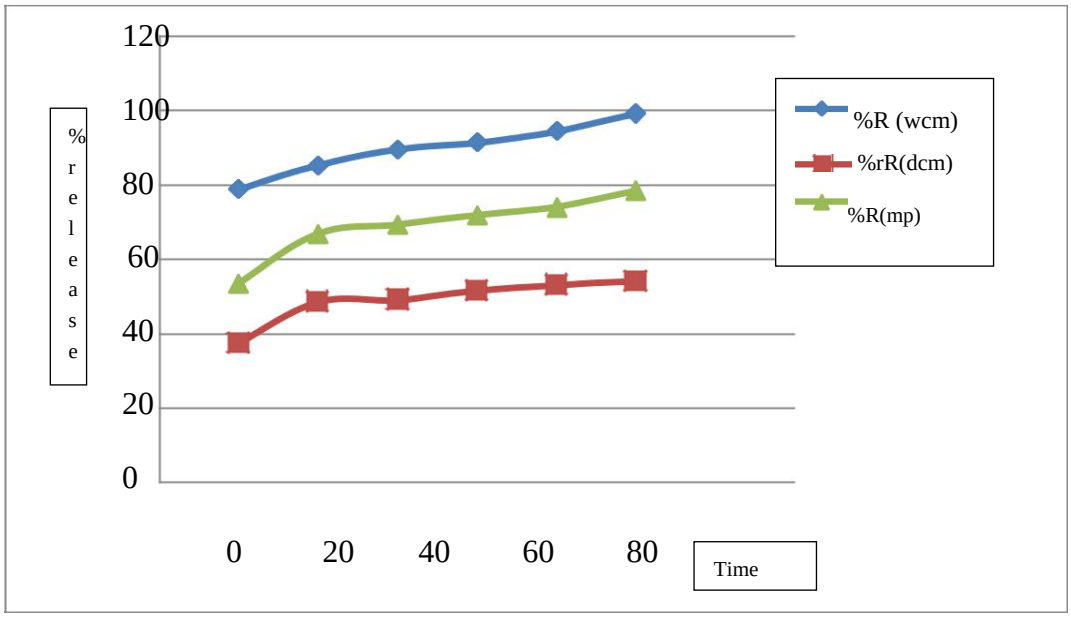

Figure 9: % releae of tablet by et granulation method, by direct compression method, and of marketed preparation.

1)%R(wcm)- % release of tablet formulated by wet granulation method.
2)%R(dcm)-% release of tablet formulated by direct compression method.
3)%R(mp)-% release of marketed preparation..

6. Summary

The main objective of the study was to developed and evaluate Immediate release and sustained release tablets of metformin using as novel dosage forms using DSP powder and polysaccharide as excipients.
Various batches were formulated the DSC studies have revealed that, there were no interaction between the drug and the excipients.
Total four batches were prepared using different proportions of drumstick powder and mucilage.

Out of all formulation studied the Batch 2 has shown the best release pattern 99.14% in 60mins (wet granulation method) in immediate release tablets.

The Drug release pattern was compared with the marketed preparations. It was found that the formulated preparartions were found to be comparable with marketed preparations as per Drug release concerned.

7. Conclusion

In the present investigation, the efforts were made to incorporate natural polysaccharide such as DS powder and polysaccharide as SR and IR agents the results of the various batches prepared were compared with the marketed preparation of ofImmediate release and sustain realease formulation.

The overall study suggested that the SR & IR tablets of metformin can be successfully developed and evaluated which would increase the bioaviability of metformin and thus these formation will be usefull in treatment of diabetic mellitus.

8. Future scope

In future sustained & immediate release tablets of metformin can be effectively formulated by using DS powder and polysaccharide. The DSP is of purely natural origin and therefore it is found to be biodegradable .The process of obtaining the natural polymer is cheap. The powder and mucilage were found to be comparatively cheaper than semisynthetic/synthetic polymer therefore ,an economical dosage form with increased bioavability of metformin can be developed and

marketed.

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