"FORMULATION AND EVALUATION OF CLOTRIMAZOLE SOLID DISPERSION FAST DISINTEGRATING TABLETS USING PALM SUGAR (*TAL MISHRI*)"

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In partial fulfillment of the requirement for the degree of

MASTER OF PHARMACY
IN
PHARMACEUTICS

Submitted by:

Saranga Shekhar Bordoloi

Reg. No: 388305219 of 2019-2020
Roll No: 190520011014

Under the supervision of:

Dr. Tapash Chakraborty (Assistant Professor)
Department of Pharmaceutics, GIPS, Ghy-17

CO-GUIDED BY:

Miss Asha Das (Assistant Professor)
Department of Pharmaceutics, GIPS, Ghy-17

GIRIJANANDA CHOWDHURY INSTITUTE OF PHARMACEUTICAL SCIENCE (GIPS), HATHKHOWAPARA, AZARA, GUWAHATI-781017, KAMRUP METRO, ASSAM (INDIA).

2021

Dedication

Dedicated to My Parents

GIRIJANANDA CHOWDHURY INSTITUTE OF PHARMACEUTICAL SCIENCE (GIPS)

(A unit of Shrimanta Shankar Academy)

Approved by AICTE & PCI, New Delhi, Affiliated to Assam Science and Technology University

N.H. 37, Hathkhowapara, Azara, Guwahati-781017

Telephone: (0361) 2843405

Email: gips_guwahati@rediffmail.com

CERTIFICATE FROM THE PRINCIPAL

This is to certify that the thesis entitled **"FORMULATION AND EVALUATION OF CLOTRIMAZOLE SOLID DISPERSION FAST DISINTEGRATING TABLETS USING PALM SUGAR (*TAL MISHRI*)."** being submitted by **SARANGA SHEKHAR BORDOLOI,** bearing **Roll no.: 190520011014 & Registration. no.: 388305219 of 2019-2020** in partial fulfilment of the requirement for the award degree of **Master of Pharmacy** (M. Pharm) **in Pharmaceutics** of the **Department of Pharmaceutics**, **Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS),** affiliated to **Assam Science and Technology University, Guwahati, Assam** is a bonafide assignment which is being carried out under my direct supervision and guidance.

Prof (Dr.) Gouranga Das
Principal,
Girijananda Chowdhury Institute of Pharmaceutical Science.
Azara, Guwahati-17

GIRIJANANDA CHOWDHURY INSTITUTE OF PHARMACEUTICAL SCIENCE (GIPS)

(A unit of Shrimanta Shankar Academy)
Approved by AICTE & PCI, New Delhi, Affiliated to Assam Science and Technology University
N.H. 37, Hathkhowapara, Azara, Guwahati-781017
Telephone: (0361) 2843405
Email: gips_guwahati@rediffmail.com

CERTIFICATE FROM THE HoD

This is to certify that the thesis entitled **"FORMULATION AND EVALUATION OF CLOTRIMAZOLE SOLID DISPERSION FAST DISINTEGRATING TABLETS USING PALM SUGAR (*TAL MISHRI*)"** being submitted by **SARANGA SHEKHAR BORDOLOI,** bearing **Roll no.: 190520011014 & Registration. no.: 388305219 OF 2019-2020** in partial fulfilment of the requirement for the award degree of **Master of Pharmacy** (M.Pharm) **in Pharmaceutics** of the **Department of Pharmaceutics**, **Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS),** affiliated to **Assam Science and Technology University, Guwahati, Assam** is a bonafide assignment which is being carried out under my direct supervision and guidance.

Dr. Bhanu Pratap Sahu
Associate Professor & HoD Pharmaceutics,
Girijananda Chowdhury Institute of Pharmaceutical Science.
Azara, Guwahati-17

GIRIJANANDA CHOWDHURY INSTITUTE OF PHARMACEUTICAL SCIENCE (GIPS)

(A unit of Shrimanta Shankar Academy)
Approved by AICTE & PCI, New Delhi, Affiliated to Assam Science and Technology University
N.H. 37, Hathkhowapara, Azara, Guwahati-781017
Telephone: (0361) 2843405
Email: gips_guwahati@rediffmail.com

CERTIFICATE FROM THE GUIDE

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Dr. Tapash Chakraborty
Assistant Professor, Dept. of Pharmaceutics
Girijananda Chowdhury Institute of Pharmaceutical Science.
Azara, Guwahati-17

GIRIJANANDA CHOWDHURY INSTITUTE OF PHARMACEUTICAL SCIENCE (GIPS)

(A unit of Shrimanta Shankar Academy)
Approved by AICTE & PCI, New Delhi, Affiliated to Assam Science and Technology University
N.H. 37, Hathkhowapara, Azara, Guwahati-781017
Telephone: (0361) 2843405
Email: gips_guwahati@rediffmail.com

CERTIFICATE FROM THE CO-GUIDE

This is to certify that the thesis entitled **"FORMULATION AND EVALUATION OF CLOTRIMAZOLE SOLID DISPERSION FAST DISINTEGRATING TABLETS USING PALM SUGAR (*TAL MISHRI*)"** being submitted by **SARANGA SHEKHAR BORDOLOI** bearing **Roll no.: 190520011014** & **Registration. no.: 388305219 of 2019-2020** in partial fulfilment of the requirement for the award degree of **Master of Pharmacy** (M. Pharm) **in Pharmaceutics** of the **Department of Pharmaceutics**, **Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS),** affiliated to **Assam Science and Technology University, Guwahati, Assam** is a bonafide assignment which is being carried out under my direct supervision and guidance during the academic session **2020-2021**.

Miss Asha Das
Assistant Professor, Dept. of Pharmaceutics
Girijananda Chowdhury Institute of Pharmaceutical Science.
Azara, Guwahati-17

GIRIJANANDA CHOWDHURY INSTITUTE OF PHARMACEUTICAL SCIENCE (GIPS)

(A unit of Shrimanta Shankar Academy)
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N.H. 37, Hathkhowapara, Azara, Guwahati-781017
Telephone: (0361) 2843405
Email: gips_guwahati@rediffmail.com

DECLARATION

I hereby declare that the thesis entitled **"FORMULATION AND EVALUATION OF CLOTRIMAZOLE SOLID DISPERSION FAST DISINTEGRATING TABLETS USING PALM SUGAR (*TAL MISHRI*)"** is a bonafide and genuine research work carried out by me under the supervision of **Dr. Tapash Chakraborty, Asst. Professor, and Asha Das, Asst. Professor, Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science,** Azara, Guwahati-17. The work embodied in this thesis is original and has not been submitted in part or full for the award of degree, diploma, associateship or fellowship of any other University or Institution.

SARANGA SHEKHAR BORDOLOI

Roll no: 190520011014
Reg. no: 388305219 of 2019-2020
Dept. of Pharmaceutics
Girijananda Chowdhury Institute of Pharmaceutical Science.
Azara, Guwahati-17

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ABSTRACT

Palms like Sugar palm, palmyra palm tree, date tree, coconut palm, raphia palm, oil palm, sago palm & nypa palm fall under the family of Arecaceae, which are well known for their sweet sap from where we get sugar. Sugar from palm is generally used locally in desserts as a sweetener. Generally, this sugar is consisting of significant amount of fructose & glucose rather than only sucrose, but still, the major palm sugar content is sucrose. Sugar obtained from palm has also been seen to having less GI (Glycaemic index) value compare to cane sugar, so this sugar has great health benefits. Many Palm products including sugar, are used in pharmaceuticals as excipients. Palm has been seen to be used as binder, starch source, oil, bioethanol, gums, super-disintegrants, nanocrystalline cellulose, microcrystalline cellulose, masking agent, etc. As we found that sugar is highly soluble in water, it can be used to form a solid solution with BCS-II classification drugs to increase the bioavailability of the drug as we know aqueous solubility is directly proportional to bioavailability. So, we can also use Palm sugar for this purpose. Clotrimazole is an anti-fungal drug. In biopharmaceutical classification system clotrimazole comes in BCS class 2 category. Being a BCS class II drug, it is very poorly soluble in water, which results in the slow dissolution and hence low bioavailability when administered orally. Oral bioavailability of a drug depends on its solubility and/or dissolution rate, therefore efforts to increase dissolution of drugs with limited water solubility is often needed. So, in the present study solid dispersion approach with Palmyra Palm Sugar used in the improvement of solubility of clotrimazole. Because Several drugs have been shown to exhibit better aqueous solubility and dissolution characteristics in the form of Solid dispersion with other type of sugars also. To overcome the low bioavailability, solid dispersion technique used to increase the bioavailability of clotrimazole, and in the fast-disintegrating tablets Solid Dispersion of Clotrimazole &

Palmyra Palm Sugar was used. Fast Disintegrating Tablets prepared by Solid Dispersion of Clotrimazole & Palmyra Palm Sugar shown good compatibility, in DSC & FTIR studies. The Solid dispersion powder has also passed all the powder characteristics tests perfectly. The tablets prepare also passed the different evaluation criterias. In in-vitro dissolution studies we also observed good cumulative drug release results, especially the tablets containing solid dispersion, which was well expected due to the increase aqueous solubility. So, Palmyra Palm sugar is a good bioavailability enhancer, it can be also used in other formulations also as solid dispersion.

LIST OF ABBREVIATIONS

Abbreviations	Full Form
FDTS	Fast disintegrating tablets
DDS	Drug delivery system
IUPAC	International union of pure and applied chemistry
Vd	Volume of Distribution
USP	United States Pharmacopoeia
BP	British Pharmacopeia
IP	Indian Pharmacopoeia
TD	Tapped density
BD	Bulk density
CI	Carr's index
RH	Relative Humidity
DSC	Differential scanning colorimetric
FTIR	Fourier transform infrared
UV	Ultra violet
%CDR	Percentage Cumulative Drug Release
AUC	Area under Curve
DT	Disintegration Time
°C	Degree Celsius
Conc.	Concentration
pH	The Negative Logarithm of the Hydrogen ion concentration
RPM	Revolution Per Minute
IR	Immediate release
HPMC	Hydroxypropylmethylcellulose
MCC	Micro crystalline cellulose

IPA	Isopropyl Alcohol
C-max	Maximum Peak Plasma Concentration
T-max	Time to achieve Peak Plasma Concentration

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CHAPTER 1- INTRODUCTION

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1.1 Solid Dosage Form:

Solid dosage forms like tablets and capsules are the most popular and preferred drug delivery systems because they have high patient compliance, relatively easy to produce, easy to market, accurate dosing, and good physical and chemical stability. Oral drug delivery has been known for decades as the most widely utilized.[1]

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is as well absorbed as the food kinds of stuff that are ingested daily. The development of pharmaceutical products for oral delivery, irrespective of physical form involves varying extents of optimization of dosage form characteristics within the inherent constraints of GI physiology. Therefore, a fundamental understanding of various disciplines, including GI physiology, Pharmacokinetics, Pharmacodynamics, and formulation design are essential to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form. The more sophisticated a delivery system, the greater is the complexity of these various disciplines involved in the design and optimization of the system. In any case, the scientific framework required successful development of an oral drug delivery system consists of a basic

Understanding of the following three aspects:

1. Physicochemical, pharmacokinetic, and pharmacodynamic characteristics of the drug.
2. The anatomic and physiologic characteristics of the GIT, and

3. Physicochemical characteristics and the drug delivery mode of the dosage form to be designed.[2]

Many patients find it difficult to swallow a tablet and hard gelatin capsule, consequently, they do not take medication as prescribed. It is estimated that 50% of the population is affected by this problem which results from a high incident of incompliance and ineffective therapy .[3]

To overcome this weakness, scientists have developed an innovative drug delivery system known as a fast-dissolving "melt in the mouth" or mouth dissolve (MD) tablet. These are a novel type of tablet that disintegrates dissolve/disperse in saliva.[4]

There are two different types of a dispersible tablet which have to be distinguished, one dosage form disintegrates instantaneously in the mouth, to be swallowed without the need for drinking water, while other tablet formulation can readily be dispersed in water, to form a dispersion, easy to ingest by the patient.[5]

Orally disintegrating tablets are also called orodispersible tablets, quick disintegrating tablets mouth dissolving tablets. Fast integrating tablets, fast-dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melt. European pharmacopeia has used the term Oro-dispersible tablet for a tablet that disperses readily and within 3 min in the mouth before swallowing.[6]

1.2 Fast disintegrating tablets.

Fast disintegrating tablets (FDTs) are those solid dosage forms when put on the tongue, disintegrate or dissolve instantaneously, releasing the drug, within a few seconds without the need of water. Fast disintegrating tablets (FDTs) aim for designing dosage forms, convenient to be manufactured and administered, free of side effects, offering immediate release and enhanced bioavailability, to achieve better patient compliance. Fast

disintegrating tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product life extension in the many elderly persons who have difficulty in taking conventional oral dosage form (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia.[7]

1.3 Requirements of fast disintegrating tablets.

The tablets should be:

- Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
- Allow high drug loading.
- Be compatible with taste masking and other excipients.
- Have a pleasing mouthfeel.
- Leave minimal or no residue in the mouth after oral administration.
- Have sufficient strength to withstand the rigors of the manufacturing process and post-manufacturing handling.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Be adaptable and amenable to existing processing and packaging machinery.
- Allow the manufacture of tablets using conventional processing and packaging equipment's at a low cost.[8]

1.4 Advantages of fast disintegrating tablets. [9-12]

FDTs offer dual advantages of solid dosage forms and liquid dosage forms along with special features which include:

- **Accurate dosing*:*** Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.
- **Enhanced bioavailability:** Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and esophagus.
- **Rapid action:** Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.
- **Patient compliance:** No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.
- **Ease of administration:** Convenient to administer especially for geriatric, pediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.
- **Obstruction free:** No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.
- **Enhanced palatability:** A good mouth feel, especially for pediatric patients as taste masking technique is used to avoid the bitter taste of drug.

- **Simple packaging:** No specific packaging required. It can be packaged in push through blisters.
- **Business avenue:** Provide new business opportunities in the form of product differentiation, line extension, uniqueness and life cycle management.
- **Cost effective:** Conventional processing and packaging equipment's allow the manufacturing of tablets at low cost.

1.5. CHALLENGES IN FORMULATION OF FAST DISINTEGRATING TABLETS (FDTS)

(I) Mechanical strength and disintegration time: It is obvious that increasing the mechanical strength will delay the disintegration time. So, a good compromise between these two parameters is always essential. FDTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. [13]

(II) Taste masking:

As most drugs are unpalatable, rapid disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance.[12-15]

(III) Aqueous solubility:

Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid

that may collapse upon drying because of loss of supporting structure during the sublimation process. Such collapse sometimes can be prevented by using various matrix-forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite.[16-17]

(IV) Hygroscopicity:

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.[18]

(V) Amount of drug:

The application of technologies used for FDTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films.[19]

(VI) Size of tablet:

It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.[20]

(VII) Mouth feels:

FDTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. Moreover, addition of flavors and cooling agents like menthol improve the mouth feel.[8]

1.6. METHOD OF PREPAIRATION OF FAST DISINTEGRATING TABLET:

(I) Freeze-drying or lyophilization[42]

It is a pharmaceutical process that allows the drying of heat sensitive drugs and biological under low temperature by the application of vacuum to remove water by sublimation. Drugs are dissolved or dispersed in aqueous solution of a carrier, transferred to preformed blister packs and subjected to nitrogen flush to freeze out, then placed in the refrigerator to complete the process. Characteristics of lyophilization techniques are, they possess high porosity and specific surface area, and gets dissolve rapidly in mouth presenting high drug bioavailability. The major drawback of this system is high cost, time-consuming procedure and fragility, making conventional packing inappropriate for packing this dosage form and stability issues under stress condition.

(II) Molding method [43]

Tablets are designed using hydrophilic ingredients, with the aim to get maximum drug dissolution. Powder mass is wetted with hydroalcoholic solvent and compressed into a dosage form. The solvent system is then allowed to evaporate. Taste of drug particles is developed by spray congealing the molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethene glycol with an active ingredient into lactose-based tablet triturate. Characteristics of molding method are, very porous as solvents are removed by drying leaving porous mass which promotes rapid dissolution.

(III) Melt granulation[44,45]

Melt granulation technique is a process by which the pharmaceutical powders are capably agglomerated by a meltable binder. The benefit of this technique compared to a conventional granulation is that no water or organic solvents is required. Since there is no drying step, the process is less time consuming and requires less energy than wet

granulation. It is a technique useful to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin.

(IV) Mass-extrusion [45]

In this the mixed ingredients are softened by water soluble ingredient i.e. polyethene glycol, using methanol as solvent, passing through an extruder to form thin cylinders. Which further get sliced with a heated blade to form small tablets. Characteristics of this method is these products can be used to mask bitter tasting drugs making small granules thus enhancing oral bioavailability.

(V) Direct compression [46]

The disintegrant addition technology (direct compression) is the most preferred technique to manufacture the tablets due to certain advantages:

- High doses can be accommodated and final weight of the tablet can exceed that of other methods.
- The easiest way to manufacture the tablets.
- Conventional equipment and commonly available excipients are used.
- A limited no. of processing steps is involved.
- Cost effectiveness.

At first the milling of the drug and excipients will be done after that sieving and mixing of drug and excipients at last compression of the tablet.

CHAPTER 1- INTRODUCTION

1.7. Solid dispersions

Solid dispersions, defined as the dispersion of one or more active pharmaceutical ingredient in a carrier at solid state and an efficient technique to improve dissolution of poorly water-soluble drugs to enhance their bioavailability. Poor water solubility is one of the major problems for the various types of drugs and various approaches have been introduced for the enhancement of solubility of such drugs. The solubility behavior of drugs remains one of the most challenging aspects in formulation development. The number of poor water-soluble compounds has dramatically increased. Currently only 10-12% of new drug candidates have both high solubility and high permeability. More than 60-65% of potent drug products suffer from poor water solubility. Solid dispersions have attracted considerable interest as an efficient means for improving the dissolution rate and hence the bioavailability of a range of hydrophobic drugs.

Compared to conventional formulations such as tablets or capsules, solid dispersions which can be prepared by various methods have many advantages. Few of the aspects are to be considered for the preparation of solid dispersions, such as selection of carrier and methods of physicochemical characterization. [21]

1.8. Method Preparation:

Melting method: In this method drug is dissolved in a suitable liquid solvent. Then, the solution is incorporated directly into the melt of polyethylene glycol obtainable below 70°c, without removing the liquid solvent. It has been shown that 5-10% (w/w) of liquid compound could be incorporated into polyethylene glycol 6000 without significant loss of its solid property. The melting method is the preparation of physical mixture of a drug and a water- soluble carrier and heating it directly until it is melted. The final solid mass is crushed, and sieved.[22]

Solvent evaporation method: The solvent evaporation method consists of the solubilization of the drug and carrier in a volatile solvent that is later evaporated.[23-24]

It involves preparation of solid dispersions by dissolving the drug in a suitable liquid solvent and then incorporating the solution directly into the melt of polyethylene glycol, which is then evaporated until a clear, solvent free film is left. The film is further dried to constant weight.[25]

Spray-drying: Spray-drying is one of the most commonly used solvent evaporation procedures in the production of solid dispersions. It consists of dissolving [26-27] or suspending the drug and carrier, then spraying it into a stream of heated air flow to remove the solvent. Due to the large specific surface area offered by the droplets, the solvent rapidly evaporates and the solid dispersion is formed within seconds [28].

Freeze-drying: This process consists of dissolving the drug and carrier in a common solvent, which is immersed in liquid nitrogen until it is fully frozen. Then, the frozen solution is further lyophilized [29]. Although it is concluded in literature that this is a promising and suitable technique to incorporate drug substances in stabilizing matrices[30], the technique is poorly exploited for the preparation of solid dispersions. An important advantage of freeze drying is that the drug is subjected to minimal thermal stress during the formation of the solid dispersion. However, the most important advantage of freeze drying is that the risk of phase separation is minimized as soon as the solution is vitrified.[31]

Co-precipitation method: Co-precipitation is a recognized technique for increasing the dissolution of poorly water-soluble drugs, so as to consequently improve bioavailability. In this method non-solvent is added drop wise to the drug and carrier solution, under constant stirring. In the course of the non-solvent addition, the drug and carrier are co-

precipitated to form micro particles. At the end, the resulted micro particle suspension is filtered and dried.[32]

1.9. Palmyra Palm

Palmyra palm (*Borassus flabellifer* Linn.) belonging to the family of *Arecaceae*, grows naturally stretching from the Persian Gulf to the Cambodian-Vietnamese boundary and is generally cultivated in India, Southeast Asia, and Malaysia, and rarely in other warm regions, including Hawaii and southern Florida. Palms are trees that profit the environment naturally, as they re-establish damaged earth, demanding very slight water in this process[33]. When the sweet juice from the budding and various materials from leaves, trunk, and underground sprouts, a slim orangish flesh covering the fibers of the completely matured fruit is eaten fresh or it is dried as a paste. The sizeable seeds, when young, before the shell solidifies, include jelly-like kernels prized as edibles. Commonly palmyra palms are tapped to make fresh or fermented drinks, syrup, and sugars. They produce sugar yields that are higher than sugarcane production. The palmyra palm (*Borassus flabellifer* Linn.) is an influential sugar-generating tree that is broadly distributed in humid Asian countries[34]. It generates sugar yield better than cane sugar [35].

Table 1: -Taxonomic Classification:

Kingdom:	**Plantae**
Clade:	**Tracheophytes**
Clade:	**Angiosperms**
Clade:	**Monocots**

Clade:	**Commelinids**
Order:	**Arecales**
Family:	**Arecaceae**
Genus:	**Borassus**
Species:	***B. flabellifer***

1.10. Sugar:

Sugar is an ace of the primogenital merchandise in the global market. It can be obtained from Sugarcane (*Saccharum officinarum*), beetroot, or other harvests having sugar content. Extensive requests of sugar make an enormous request in the native plus in the global marketplace. A valuation of the ecological effect for the sugar manufacturing for business has done in terms of manufacture, dispensation, reusing, and application. The sugarcane industry has an important influence on government income and services. Additional benefits like the growth of public schemes and organizational features of the ecological administration plan. The drive of the learning to emphasize the position of the sugar manufacturing with the process, the resource essential and goods formed along with bases of contamination and built-in justification measures regarding effluent, smoky emissions, and dense wastes. The sugar manufacturing side-products are now being utilized as fresh material in the manufacturing of valued products, which offers service to the countryside public and also has the probable to earn counterfeiting argument by the exportation. This displays that the sugar business did not include in a cohort of damaging chemical material neither the product disturbs the nearby atmosphere. It comes

under the green industry, which kept zero release [36]. Sugars as excipients have many claims, for example, they are used in compressed tablets and other dosage forms also. Mostly helpful as excipients as compressible sugar (sucrose), sugar esters, sugar laurate, crystalline malt sugar, sugar alcohol (mannitol), and D-glucose. Initially, sugar-based excipients were applied for hiding the awful taste. Recently, they are found to help elevate compressibility or used for their hydrophilic/hydrophobic properties and included in nanosuspension & particles as sugar esters. The word sugar describes the chemical class of carbohydrates (qv) of the general formula Cn (H2O) n1 or (CH2O) n for monosaccharides. Colloquially, sugar is the common name for sucrose, the solid crystalline sweetener for foods and beverages. Sucrose, a disaccharide, is found in most plants, but is in sufficient concentrations for commercial recovery only in sugarcane and sugar beet plants. Sucrose [57-50-1] (b-D-fructofuranosyl-a-D-glucopyranoside), C12H22O11, formula weight 342.3, is a disaccharide composed of glucose and fructose residues joined by an a,b-glycosidic bond [37]

1.11. Properties of Sugar:

The physical and functional characteristics of sugars, chiefly sucrose, in diets and drinks are seen that chief functional characteristics of sugars comprise of sweetener action, as a flavour garnish and constant, antioxidant and antibacterial, and contact with water to impact water action. Chemical reactions comprise Maillard reactions or browning compound formation, caramelization, and fermentation. In drinks, properties of sugariness and flavour are significant. Solubility is especially significant in fermented beverages. Elevations and features of non-sugars current in the sweeteners can touch the arrival, flavour, and constancy of a drink [38].

CHAPTER 1- INTRODUCTION

1.12. Drug Profile:

1.12.1 Name: Clotrimazole.

1.12.2 IUPAC Name: 1-[(2-chlorophenyl) diphenyl methyl]-1*H* imidazole.

1.12.3 Chemical Formula: $C_{22}H_{17}CIN_2$.

1.12.4 Chemical Structure:

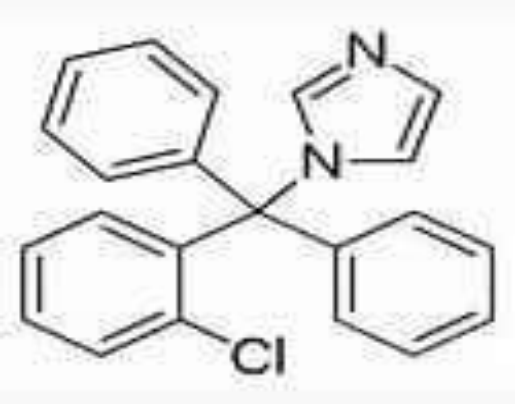


Fig 1: Molecular structure of Clotrimazole

1.12.5 Molecular Weight: 344.8 g/mol.

1.12.6 Solubility: Sparingly soluble in ether and very soluble in polyethylene glycol 400, chloroform, DMF, DMSO, and sparingly soluble in aqueous buffer and practically insoluble in water.

1.12.7 Absorption

Topical: negligible through intact skin.

Time to peak serum:

Oral, topical: Salivary levels occur within 3hrs after 30min dissolution time.

Vaginal cream: High vaginal levels: 8-24 hrs.

1.12.8 Route of elimination: Feces (as metabolite)

1.12.9 Side effects

Oral tablets:

G.I: Nausea, vomiting

Vaginal:

Genitourinary: Vaginal/vulvar bleeding

Burning or itching of penis of sexual partner polyuria; vulvar itching, soreness, edema, soreness, edema, discharge.

CHAPTER 2- LITERATURE REVIEW

CHAPTER 2- LITERATURE REVIEW

REVIEW OF LITERATURE

1. Madgulkar *et al.*, (2015): Tablet weighing 500 mg each, containing solid dispersion equivalent to 100 mg of clotrimazole at various drug to sugar ratios 1:3, 1:1 and 3:1 using mannitol, fructose, dextrose and maltose as selected sugars were prepared. Tablets containing pure drug (100 mg) were also prepared by direct compression method. Microcrystalline cellulose, crospovidone, aerosil and magnesium stearate were used as directly compressible diluent, super disintegrant, lubricant and glidant, respectively. All ingredients were mixed thoroughly and compressed by direct compression method. The solubility, dissolution rate and antifungal activity of clotrimazole were improved by solid dispersion with mannitol and fructose. Saturated solution of mannitol increases the solubility of clotrimazole 806 times as compared with plain clotrimazole (0.49 mg/mL). Also, dissolution profile of **clotrimazole** was enhanced by mannitol solid dispersion. This has resulted into enhanced antifungal activity of the drug in mannitol **solid dispersion** [60].

2. Surendran *et al.*, (2013): Solid dispersions of **clotrimazole** in β cyclodextrin containing three ratios (1:1, 1:2, 1:3 w/w) were prepared by kneading method. Here beta-cyclodextrin was taken in mortar and little amount of ethanol was added and triturated to obtained a homogenous slurry like consistency. Slowly the drug was incorporated into the slurry, and trituration was continued for 1 hour and then dried at 250 C for 24 hours, pulverized, sieved through mesh no.100. In-vitro drug release of clotrimazole solid dispersion incorporated gels has been evaluated, it founded the best release compared to other formulated gels [41].

3. Balata *et al.*, (2011): Clotrimazole and β-Cylodextrin with and without the addition of hydrophilic polymers were dissolved at 40° in the lowest volume of 50% ethanol

(which is necessary to obtain solution) and stirred for 30 min. Then, the solvent was evaporated in a vacuum oven at 50° until complete drying was obtained as shown by constant weight. The dried mass was pulverized, passed through 60-mesh size sieve and stored in a desiccator until used for further studies. β-Cyclodextrin alone yielded a 3-fold increase in the solubility of clotrimazole [42].

4. Srikaeo *et al;* (2019): Palm sugar is a valuable nutritional product which is produced by dehydrating palm sap until it reaches the desired solid concentrations. It can be produced in various forms, such as syrup and powder. As palm sugars are processed minimally, they retain natural phytonutrients, which possess many biological functions with beneficial effects on human health. Palm sugars, including similar types, e.g., coconut sugars, have been reported to exhibit lower GI values than refined cane sugars. Palm sugars contain significant amounts of other sugars, such as fructose and glucose, rather than only sucrose, as shown before. Although the major sugar component in palm sugars is sucrose, similar to cane sugars. However, it should be noted that consumption of large amounts of any sugars could lead to health risks [43].

5. Das *et al;* (2011): The dissolution of the poorly aqueous soluble drug, etoricoxib was increased by solvent evaporation technique using various sugar carriers, such as lactose, sucrose, and mannitol. Etoricoxib solid dispersions and their respective physical mixtures using lactose, sucrose, and mannitol were prepared in different ratios by solvent evaporation technique. The saturation solubility and in vitro dissolution studies showed a remarkable increase compare to the pure drug [44].

6. Merwe *et al;* (2020): Sugars as excipients have many claims, for example, they are used in compressed tablets and other dosage forms also. Mostly helpful as excipients as compressible sugar (sucrose), sugar esters, sugar laurate, crystalline malt sugar, a

sugar alcohol (mannitol), and D-glucose. Initially, sugar-based excipients were applied for hiding the awful taste. Recently they are found to help elevate compressibility or used for their hydrophilic/hydrophobic properties and included in nanosuspension & particles as sugar esters [45].

7. Sapurto *et al;* (2019): Sugar obtained from the palm is an ordinary sweetening agent obtained from sap/nectar composed from the florae of many classes of various types of palms like *Arenga pinnata*, *Borassus flabellifer*, *Phoenix dactylifera L.*, *Cocos nucifera,* etc all belong to the family of *Arecaceae*. This sweetener has been utilized as a common and substitutes sweetener in the Southeast and South Asian counties, such as Indonesia, Philippines, Thailand, Malaysia, and India in such counties, the various types of palm trees are grown naturally in abundance. Countries like Indonesia and the Philippines are the main palm sugar manufacturers on the globe. Sugar from the palm is mostly utilized in soy sauce, drinks, sweets, and numerous items of traditional diets. Its usage is considerably enjoyed and acknowledged for the sense of taste, color & flavor progress of the delicacies. Sugar from the palm is primarily utilized in soy sauce, cuisines and beverages, candies, and numerous pieces of stuff of traditional foods. Its usage is very considerable and acknowledged for the good taste, colour characteristics, and also flavour progress of the beverages and diets. The usage of sugar obtained from palm trees as soybean sauce sweetener extremely affects the soybean sauce taste due to the presence of extra 70 essential oils. The usage of sugar from palm also affects the textural characteristics, appearance, and flavor of cookies [46].

8. Gardner *et al;* (2017): The palm syrup is obtained from naturally grown palm trees. Maximum of these molasses is generally consumed and usually produced as bottled juice as the bottled juice from the palm tree, palm wine, palm sweeteners. Since pure

palm syrup is having a content of higher amounts invert sugar, it's fairly tough to progress or convert into novel products which make the higher cost than the current products (4). Cane sugar is still the widely utilize sugar, but they cause a health problem. Sugar alcohols like mannitol have low calories but it's not quite economical to use. Palm and coconut sugars could be healthier in terms of GI value compared to cane sugar [47].

9. Ngwuluka *et al*; (2010): Dried date palm fruit is a natural product that is non-toxic, biodegradable, and biocompatible that can be employed as a pharmaceutical binding agent for immediate release dosage forms. The granules manufactured with date palm had good flow properties and satisfactory compressibility which led to tablets with less variation in uniformity. The tablets had good uniformity of weight, thickness, and diameter, hard and less friable than acacia and tragacanth as its concentration increases; and a better binder than tragacanth [48].

10. Al-Remawi *et al;* (2017): Date trees contain crucial substances that can give easily as pure date palm cellulose and so instead of burning the dead trees their cellulose which can used conventionally in pharmaceutical industry. Brine seawater contains essential divalent cations which produces water-insoluble silicate salts of calcium and magnesium upon reacting with sodium silicate) which is an inexpensive product of sand silica and soda). Thus, it is possible to produce mineral-fibre solid dispersion through the inclusion of water-insoluble silicate salts within the date palm cellulose and so improving date palm cellulose compaction and disintegration properties. The tablets produced using water-insoluble calcium with magnesium silicate salts and date cellulose were tougher and had lesser disintegration time at all compression forces compared to those made with date palm cellulose. The produced excipient had excellent compaction and disintegration properties and could be used as a super disintegrant and tablet binder in pharmaceutical industries [49].

11. Sahari *et al;* (2012): Bioethanol is a raw material for many products like chemicals, solvents, pharmaceuticals, cosmetics, medicines, and beverages. The palm "*Arenga pinnata*" is a versatile tree grown in Malaysia. Besides producing sugar, it is used for products like ropes, filters, sweepers, and rooftop materials. Nowadays, researchers finding new ways to produce ethanol, which can obtain from its sugar [50]**.**

12. Walsh *et al;* (2014): Sucrose is having the best taste masking abilities no influence in the wanted instant release profile. The masking could be further improved by using Witocan H, which is a triglyceride based on coconut/palm (Cocos nucifera) kernel oil instead, but the addition of the Benecoat BMI-40 bitterness suppressant is needed [51].

13. Sopyan *et al;* (2020): Owing to the fascinating behavior of nanocrystal cellulose like biocompatibility, non-toxicity, hydrophilic nature as well as self-assembly in the liquid state, it has been extensively employed as an emulsifier, thickener, cosmetics, and pharmaceutical applications. Nanocrystal cellulose derived from sugar palm (*Arenga pinnata*) bunches are qualified in all the criteria, to be used as binders & fillers in the tablets [52].

14. Chaerunisaa *et al*; (2020): MCC is a famous excipient which is mostly utilize in pharmaceutical formulations. It has application for binder, disintegrant, absorbent, diluent, lubricant & anti-adherent. Its high utilization for microcrystalline cellulose in pharmaceutical formulations have led in the search for organic materials to produce microcrystalline cellulose. Oil palm (*Elaeis guineensis*) biomass and leaves can be applicable for a good source of MCC [53].

15. Builder *et al*; (2016): Starch is one of excipient used in manufacturing of tablets. Chemically, starches are polysaccharides, composed of various monosaccharides or sugar (glucose) molecules linked together with α-d-(1-4) and/or α-d-(1-6) linkages.

CHAPTER 2- LITERATURE REVIEW

Starch is examined as a good excipient in new drug delivery classifications for nasal delivery, oral delivery, periodontal delivery, and other site-specific carrier systems. Based on applications, particular starches are accessible as a disintegrants, diluents or binders. Sago starch is an unofficial starch obtained from the sago palms (Metroxylon sagu Rottb.), the physicochemical properties and its potential for use as a body powder and lubricant in certain surgical and diagnostic materials has been studied & investigated [54].

CHAPTER 3- AIM & OBJECTIVE

CHAPTER 3- AIM & OBJECTIVE

AIM: Formulation and Evaluation of Clotrimazole Solid Dispersion Fast Disintegrating Tablets using Palmyra Palm Sugar (*Tal Mishri*).

OBJECTIVE

The objective of the present work is to:

- Obtaining of pure Palm sugar (Tal Mishri) from market.
- Preparation of solid dispersion of the drug.
- Preparation of the fast-disintegrating tablet.
- Evaluation of the tablet formulation.

PLAN OF WORK

- literature review on national and international context.
- Obtaining of Palm sugar (*Tal Mishri*) from the market.

1. Preparation Solid dispersion of the drug.

- Solvent evaporation method.

2. Pre formulation parameters:

- Organoleptic properties.
- Solubility.
- UV-Spectrophotometry.
- Compatibility study by DCS and FTIR.

CHAPTER 3- AIM & OBJECTIVE

3. Formulation of fast disintegrating tablet.

Fast disintegrating tablet will be prepared using direct compression technique.

4. Post compression parameter

- Physical parameters
- Organoleptic properties.
- Weight variation test.
- Friability.
- Hardness.
- Drug content uniformity.
- *In-Vitro* disintegrating time.
- *In-Vitro* dissolution time.
- *Ex-Vivo* Absorption Study by Cell-diffusion method.

CHAPTER4- MATERIALS AND METHODS

CHAPTER 4- MATERIALS & METHOD

5. METHODOLOGY:

LIST OF CHEMICALS USED:

Ingredients	Source
Clotrimazole	GIPS, Chemical Store
Palm Sugar	Azara market
MCC	Krishna, Enterprise, Bhatta, Budling, Panbazar, Guwahati
Magnesium stearate	BS. Trading Rabindra, Sarani, Howrah
Crospovidone	S. D. Fine Chemicals Ltd., Mumbai, India
Ethanol, Glacial Acetic Acid	BS. Trading Rabindra, Sarani, Howrah
Acetone, methanol	Krishna Enterprise, Bhatta Budling, Panbazar Guwahati
Whatman filter paper	S. D. Fine Chemicals Ltd., Mumbai, India
Aerosil, HCL, Phosphoric Acid	GIPS, Chemical Store

Table 2: Excipient will be used in the formulation.

INATRUMENT TO BE USED IN PRESENT WORK:

Instrument	Make and Model
UV Spectrophotometer	Shimadzu 1700, UV-Visible spectrophotometer, Japan
Dissolution test apparatus	Dissolution test apparatus-TDT-06T, Electrolab, Mumbai, India.

Ph meter	Systronic, 361-micro pH meter
Balance	Sartorious electronic balance
Roche Friabilator	Camp-bell Electronics, Mumbai, India

Table 3: Instrument to be used in Research Work.

1. PREFORMULATION STUDY OF THE DRUG:

1.1 The organoleptic properties:

color, odor, taste was evaluated. [3]

1.2 Solubility study:

A minute quantity of the drug was taken on a test tube and the solubility of the drug was determined by dissolving the drug in 10 ml of various solvents like water, acetone, methanol, ethanol, chloroform, glacial acetic acid etc. [1]

1.3 Melting point:

A little amount of the drug sample in a dry capillary tube of 1 mm internal diameter forming a column about 3mm high. Heat the melting point apparatus to a temperature 5-10 0c below the expected temperature of melting and adjust the heating so that the temperature in the chamber rises about 10 °C per minute. [2-3]

1.4 Fourier Transform Infrared Spectroscopy (FTIR):

The FT-IR analysis of the pure drug, excipients, drug-excipients will be carried out with FT- IR instrument (Bruker 10059736).

1.5 Differential Scanning Calorimetry (DSC):

DSC can be used to determine the nature and specification of crystallinity of drug and excipients through measurement of glass transition temperature and melting point temperature and their associated enthalpies. This technique has been used to study the physical and chemical interaction between drug and excipients. About 5- 7 mg amount of drug, taken and then the samples will be sealed in aluminum pans analyzed in an atmosphere of air flow rate 25ml/min. A temperature range of 30 °C to 340 °C was used where the rate of heating is 10 ^{0}C/min.[4] In the DSC apparatus (Mettler) is used.

1.6 Preparation of standard calibration curve of Clotrimazole in 0.1 N HCl:

The stock solution was prepared by dissolving 100 mg of drug in 100 ml of 0.1 N HCL to get 1 mg/ml concentration. Suitable aliquots were diluted to obtain solution of 2 ug/ml, 4 ug/ml, 6ug/ml, 8ug/ml, 10ug/ml. The absorbance of each solution measured at the absorption maxima using 0.1 N HCL as blank at 264 nm. The standard curve will be obtained by plotting the observed absorbances with the respective concentrations. [5]

1.7 Preparation of the Solid dispersion of the drug:

Solvent evaporation method: The solvent evaporation method consists of the solubilization of the drug and carrier in a volatile solvent that is later evaporated. It involves preparation of solid dispersions by dissolving 5gm of drug (Clotrimazole) and 5gm of excipient (Palm Sugar) in a suitable liquid solvent of 100ml (Ethanol) which is then evaporated until a clear, solvent free film is left. The film is further dried to constant weight. The film was scratched from the Petri dish and it was pulverized into powder which was passed through sieve no.60, to obtain fine 1:1 ratio powder of solid dispersion [6].

CHAPTER 4- MATERIALS & METHOD

2. PREPAIRATION OF FAST DISINTEGRATING TABLET OF CLOTRIMAZOLE

Clotrimazole Fast Dissolving tablet is prepared by direct compression method using various, Microcrystalline Cellulose, Magnesium stearate, Crospovidone, aerosil. Tablet weighing 500 mg each, containing solid dispersion equivalent to 100 mg of CTZ at drug to sugar ratios 1:1 using palm sugar prepared. Tablets containing pure drug (100 mg) were also prepared by direct compression method. Microcrystalline cellulose, crospovidone, aerosil and magnesium stearate were used as directly compressible diluent, super disintegrant, lubricant and glidant, respectively. All ingredients were mixed thoroughly and compressed by direct compression method. Tablet compression machine (Shakti Pharmatech Pvt Ltd.) with die size 12 mm flat was used [7].

3. PRE-COMPRESSION PARAMETERS [9]:

3.1. Angle of repose (θ):

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose.

$\tan \theta = h / r$

$\Rightarrow \theta = \tan^{-1} (h/r)$

Where, θ is the angle of repose h-height of pile

r- radius of the base of pile.

Relationship between angle of repose (θ) and flow properties.

Angle of repose(θ)(degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Table 3- Ranges of Angle of Repose.

Method: A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on a graph sheet was taken to measure the area of pile, thereby evaluating the flow ability of the granules. Height of the pile was also measured.

3.2. Bulk density:

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another.

Method: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of accurately weighed powder (bulk) from each formula, previously shaken to break any agglomerates formed was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5cm at 2 sec intervals. The taping was continued until no further change in volume was noted. LBD and TBD were calculated using following formula;

$$LBD = \frac{\text{Weight of powder}}{\text{Volume of packing}} \quad \text{----------(a)}$$

$$TBD = \frac{\text{Weight of powder}}{\text{Tapped packing}} \quad \text{----------(b)}$$

3.3. Percentage Porosity: This can be calculated by taking the value of bulk density and true density

$$\text{Percent Porosity} = 1 - \frac{\text{Bulk density}}{\text{True density}} \times 100$$

3.4. Carr's Index (CI):

Tapped and bulk density measurements can be used to estimate the Carr's index of a material. Carr's index was determined by:

Carr's Index (%) = {(Tapped density – Bulk density)/ Tapped density} × 100

Carr's Index	Flow
5-15	Excellent
12-16	Good
18-21	Fair

23-35	Poor
35-38	Very Poor
More than 40	Extremely Poor

Table 4: Standards for Carr's Index.

3.5. Hausner's Ratio (HR):

It is stated by Hausner. It was calculated as follows:

Hausner's Ratio = Tapped density/Bulk density.

Hausner's Ratio (H.R)	Flow
1.2–1.3	Excellent
1.3–1.4	Good
1.4–1.5	Fair
1.5–1.6	Poor

Table 5: Standards for Hausner's Ratio.

4. POST-COMPRESSION PARAMETERS:

4.1. All the formulation of clotrimazole prepared were evaluated for the following physical and organoleptic parameters:

Physical Parameters:

- Size & shape

CHAPTER 4- MATERIALS & METHOD

Organoleptic Parameters:

- Color, taste & odor.

4.2. Tablet Properties:

4.2.1. Hardness test:

Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The hardness of the tablets will be determined using Monsanto Hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked from each formulation and the mean and standard deviation values will calculated.

4.2.2. Friability test:

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Veego Friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed (W-initial) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or n up to 100 revolutions. The tablets were weighed again (W-final). The percentage friability was then calculated by:

$$F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

% Friability of tablets less than 1% is considered acceptable.

4.2.3. Weight variation test: [10]

The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

Average weight of a tablet	Percentage deviation
130mg or less	10
More than 130mg and less than 324mg	7.5
324mg or more	5

Table 6- Weight variation standard table.

4.2.4. Drug content uniformity: [11]

Twenty tablets were weighed and crushed in a mortar. Then weighed powder contain equivalent to 100mg of drug transferred in 100ml of 0.1 N HCL. Its concentration

1000 µg/ml. 10ml from this stock solution taken and diluted to 100ml of 0.1N HCL, it makes 100µg/ml. Then 0.6ml from stock solution and diluted to 10ml. Absorbance measure at 264 nm.

4.2.5. In vitro disintegration time: [6]

The process of breakdown of a tablet into smaller particles is called as disintegration. The in-vitro disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications.

I.P. Specifications: Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using 0.1 N HCL maintained at 37°±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the 0.1 N HCL maintained at 37°±2°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus will be measured and recorded.

4.2.6. In vitro dissolution studies: [6]

Dissolution rate was studied by using USP type-II apparatus at 50 rmp using 900ml of 6.8 phosphate buffer Temperature of the dissolution medium was maintained at 37±0.5°C, aliquot of dissolution medium was withdrawn at every 1 min interval and filtered. The absorbance of filtered solution was measured by UV spectrophotometric method at 264 nm and concentration of the drug was determined from standard calibration curve.

- **In vitro drug release studies details:**

(I) Apparatus used: Dissolution test apparatus.

(II) Dissolution medium: 0.1 N HCL.

(III) Dissolution medium volume: 900 ml.

(IV) Temperature: 37 ± 0.5°C.

(V) Speed of basket paddle: 50 rpm.

(VII) Sampling intervals: 1 min.

(VIII) Sample withdraws: 5 ml.

(IX) Absorbance measured: 264 nm

CHAPTER 5- RESULTS AND DISCUSSION

CHAPTER 5- RESULT & DISCUSSION

RESULTS:

1. Preparation of Solid Dispersion:

Figure 2: Clotrimazole & Palmyra Palm Sugar were mixed together in Mortar which were taken Mixed in 1:1 by taking 5gm each.

Figure 3: After being sieved by sieve no. 60 was dissolved in 90%, ethanol at 25°C, on a hot magnetic stirrer at 50 RPM.

Figure 4: After heating for 1 hour a white slurry type of solid film has been observed at the bottom of the beaker.

Figure 5: Then the remaining solvent was evaporated in hot air oven to make it drier & powder like, so it can be incorporated in tablets.

CHAPTER 5- RESULT & DISCUSSION

Figure 6: **Then the dried powder was sieved by sieve no. 60, to get fine powder of the solid dispersion.**

Figure 7: **Fine powder was produced of solid dispersion was produced, which was white in color.**

2. Organoleptic properties:

2.1 Organoleptic properties of Clotrimazole:

Drug	State	Color	Odor	Taste
Clotrimazole	Solid	White/Pale Yellow	odorless	No Taste

Table 7: **Organoleptic properties of pure drug (Clotrimazole).**

2.2 Organoleptic properties of Palmyra Palm Sugar:

Excipient	State	Color	Odor	Taste
Palmyra Palm Sugar	Solid	Yellowish Golden Color	Fruity Sweet Smell	Sweet

Table 8: **Organoleptic properties of pure excipient (Palmyra Palm Sugar).**

CHAPTER 5- RESULT & DISCUSSION

2.3 Organoleptic properties of Solid Dispersion of Clotrimazole & Palmyra Palm Sugar:

Solid Dispersion	State	Color	Odor	Taste
Palmyra Palm Sugar & Clotrimazole	Solid	Slightly Brownish White	Slightly Fruity to odorless	Slightly Sweet

Table 9: Organoleptic properties of Solid dispersion (Palmyra Palm Sugar & Clotrimazole).

3. Physicochemical characterization of drug:

3.1 Solubility of Clotrimazole: Soluble in Ethanol, DMSO, Acetone, chloroform, Ethyl Acetate & slightly soluble in Water, Benzene, Toluene, Ether.

3.2 Solubility of Palmyra Palm Sugar: Soluble in Water, Ethanol, DMSO, Acetone & slightly soluble in Chloroform & Ethyl acetate, but not soluble in Benzene, Toluene & Ether.

3.3 Solubility of Solid Dispersion: Soluble in Ethanol, Water, Acetone, Ethyl Acetate, DMSO, but slightly soluble in Chloroform, Ethyl Acetate, Benzene, Toluene & not soluble in Ether.

4. Melting point:

4.1 Clotrimazole: The melting point of the pure drug sample of Clotrimazole was found to be 140.48 °C to 144.52 °C.

CHAPTER 5- RESULT & DISCUSSION

4.2 Palmyra Palm Sugar: The melting point excipient sample of sugar was found to be 180.48 °C to 188.70 °C.

4.3 Solid Dispersion: The melting point solid dispersion of Palmyra palm sugar & Clotrimazole is 176.18 °C to 188.80 °C.

5. Standard curve of Clotrimazole in 0.1 N HCL:

Table 10: Preparation of calibration curve of Clotrimazole with 0.1N HCL.

Serial no.	Concentration (µg/ml)	Absorbance (nm)
1	2	0.0209
2	4	0.0846
3	6	0.1334
4	8	0.1813
5	10	0.2466

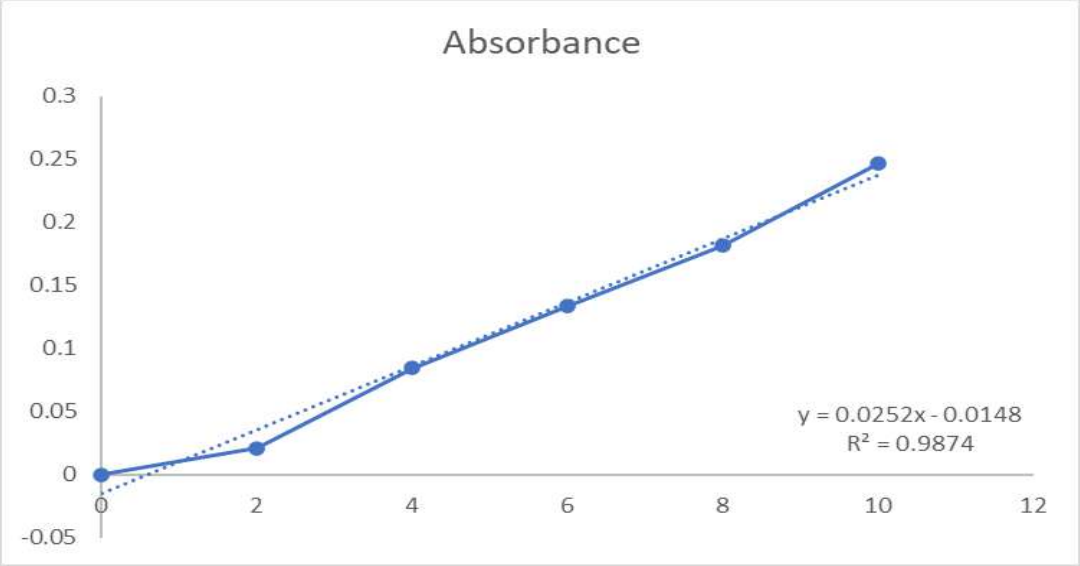


Fig 8: Standard calibration curve of Clotrimazole in 0.1N HCL at λ max at 264 nm.

CHAPTER 5- RESULT & DISCUSSION

6. Fourier Transform Infrared Spectroscopy (FTIR):

6.1. FTIR of Clotrimazole:

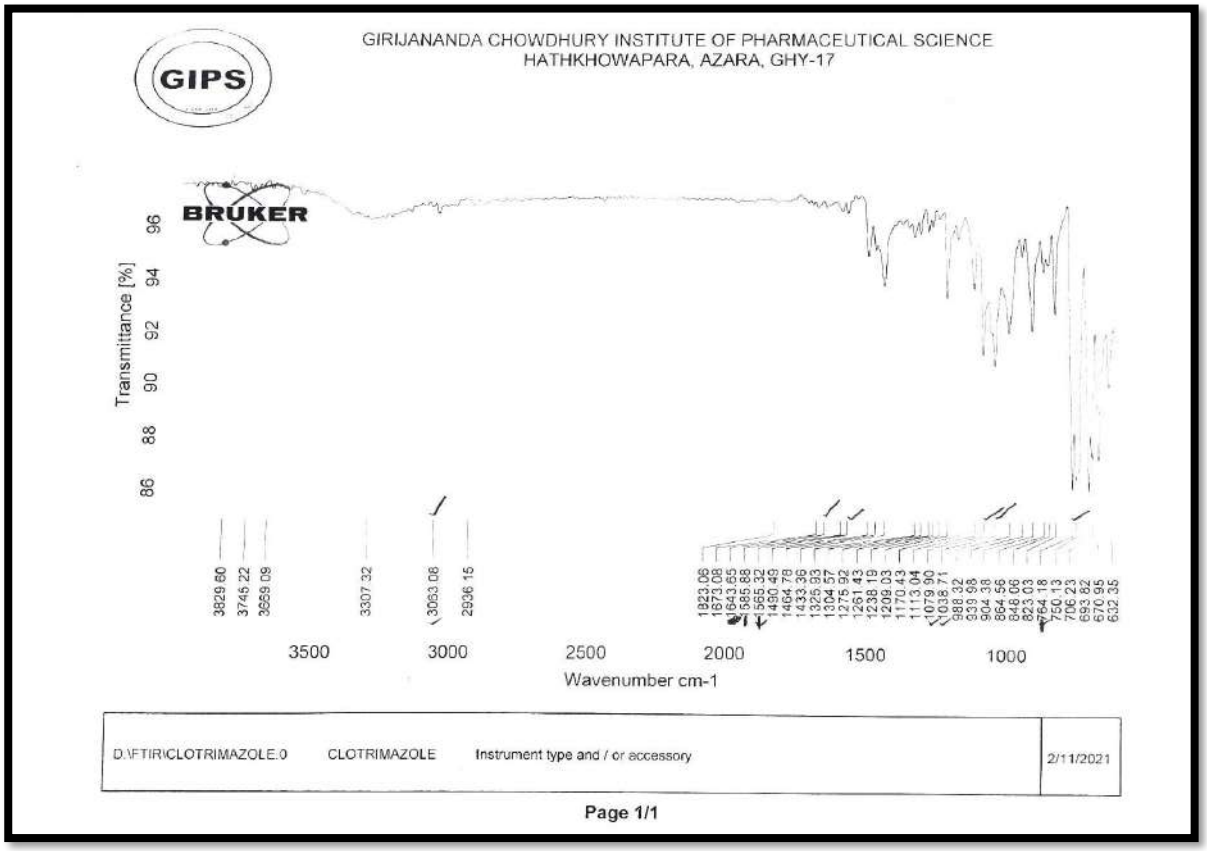


Figure 9: FTIR spectra of Clotrimazole.

Wave number (cm^{-1})	Functional Group	Compound
3829.60	None	None
3745.22	None	None
3669.09	None	None
3307.32	N-H stretching	Aliphatic primary amine
3063.08	C-H stretching	Alkene
2936.15	O–H stretch	Carboxylic acids
1823.06	None	None
1673.08	C=C stretching	Alkene

1643.65	C=N stretching	Imine / Oxime
1585.88	N-H bending	Amine
1565.32	C=C stretching	Cyclic alkene
1490.49	N–O asymmetric stretch	Nitro compounds
1464.78	C–H bend	Alkanes
1433.36	C–C stretch (in–ring)	Aromatics
1325.93	S=O stretching	Sulfone
1304.57	N-O stretching	Nitro compound
1275.92	C–N stretch	Aromatic amines
1261.43	C–N stretch	Aromatic amines
1238.19	C-O stretching	Alkyl aryl ether
1209.03	C-O stretching	Tertiary alcohol
1170.43	C-O stretching	Ester
1113.04	C-O stretching	Secondary alcohol
1079.90	C-O stretching	Primary alcohol
1038.71	S=O stretching	Sulfoxide
988.32	C=C bending	Alkene
939.98	O–H bend	Carboxylic acids
904.38	None	None
864.56	C=C bending	Alkene
848.06	C=C bending	Alkene
823.03	None	None
848.06	C=C bending	Alkene
823.03	None	None
764.18	C=C bending	Alkene
750.13	–C≡C–H: C–H bend	Alkynes
706.23	C–H “oop”	Aromatics

693.82	–C≡C–H: C–H bend	Alkynes
670.95	–C≡C–H: C–H bend	Alkynes
632.35	–C≡C–H: C–H bend	Alkynes

Table 11: FTIR of Clotrimazole.

6.2. FTIR of Palmyra Palm Sugar

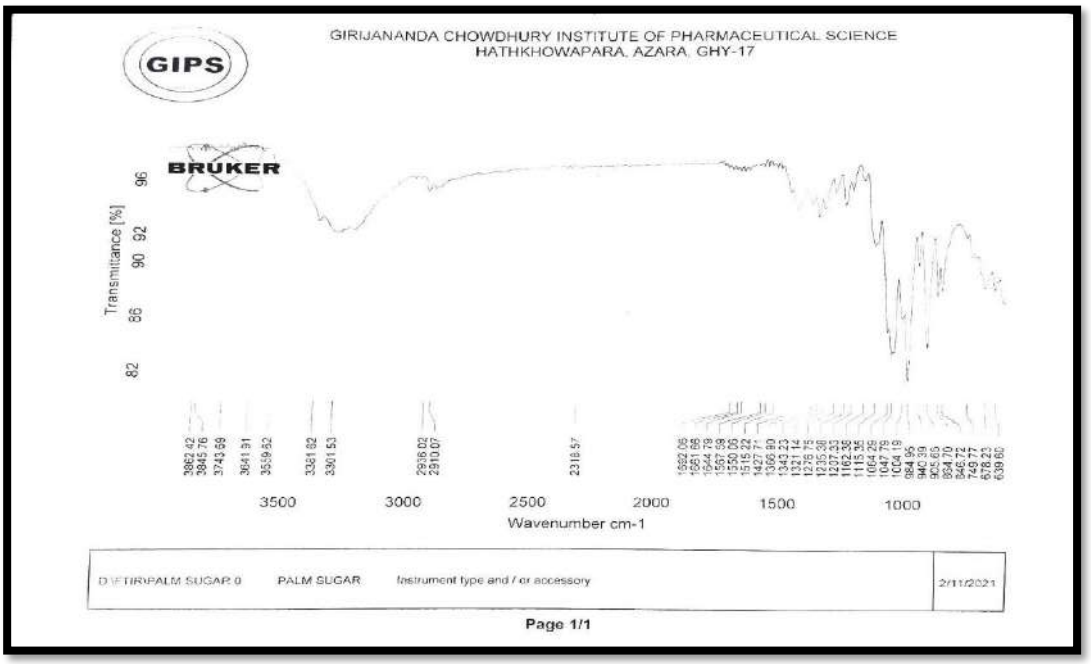


Figure 10: FTIR Spectra of Palmyra Palm Sugar

Wave number (cm-1)	Functional Group	Compound
3862.42	None	None
3845 .76	None	None

3743 .69	None	None
3641.91	None	None
3559.62	O-H stretching	Alcohol
3381.62	N-H stretching	Aliphatic primary amine
3301.53	N-H stretching	Aliphatic primary amine
2936 .02	None	None
2910.07	None	None
2318.57	None	None
1692.06	C=O stretch	carboxylic acids
1661 .66	C=C stretching	Alkene
1644.79	C=N stretching	Imine / Oxime
1567.59	C=C stretching	Cyclic alkene
1550.06	N-O stretching	Nitro compound
1515.22	N-O stretching	Nitro compound
1427.71	O-H bending	Alcohol
1366.90	None	None
1343.23	S=O stretching	Sulfonic acid

1321.14	S=O stretching	Sulfonic acid
1276.75	None	None
1235.38	None	None
1207.33	C-O stretching	Vinyl ether
1115.35	C-O stretching	Secondary alcohol
1064.29	C–O stretch	Alcohols, carboxylic acids, esters, ethers.
1047.79	C–N stretch	Aliphatic amines
1004.19	C–O stretch	Alcohols, carboxylic acids, esters, ethers**.**
984.95	None	None
940.39	O–H bend	Carboxylic acids
905.65	None	None
864.70	C=C bending	Alkene
846.72	C=C bending	Alkene
749.77	None	None
678.23	C–H	Aromatics
639.60	–C≡C–H: C–H bend	Alkynes

Table 12: FTIR of Palmyra Palm Sugar.

6.3. FTIR of Solid Dispersion:

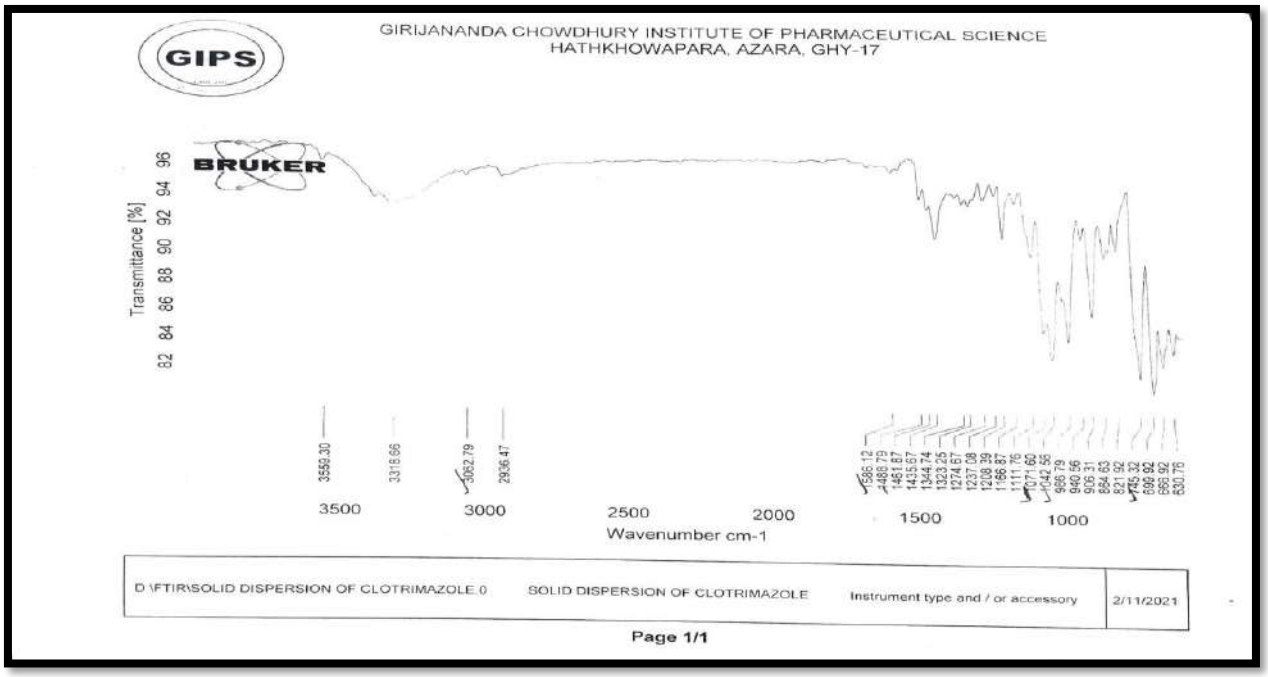


Figure 11: FTIR Spectra of Solid Dispersion.

Wave number (cm-1)	Functional Group	Compound
3559.30	O-H stretching	Alcohol
3318.66	N-H stretching	secondary amine
3062.79	C-H stretching	Alkene
2936.47	C-H stretching	Alkyne

1586.12	N-H bending	Amine
1488.79	O-H bending	Alcohol
1461.87	C–H bend	Alkanes
1435.67	C–C stretch (in–ring)	Aromatics
1344.74	N–O symmetric stretch	Nitro compounds
1323.25	C–N stretch	Aromatic amines
1274.67	N–O symmetric stretch	Nitro compounds
1237.08	C–N stretch	Aliphatic amines
1208.39	C-O stretching	Vinyl ether
1166.87	C-O stretching	Ester
1111.76	C-O stretching	Secondary alcohol
1071.60	None	None
1042.56	C–C stretch (in–ring)	Aromatics
986.79	C=C bending	Alkene
940.56	O–H bend	Carboxylic acids
906.31	None	None
864.63	None	None
821.92	C–Cl stretch	Alkyl halides

745.32	None	None
699.92	None	None
666.92	None	None
630.76	None	None

Table 13: FTIR of Solid Dispersion

7. DSC Results of Samples:

We see that each drug is giving you some melting point. Plus, the excipient s also is giving certain peaks of melting point. So, after mixing the drug & excipient. The melting point of drug should not change drastically and must be in range of what we have checked have checked there is no such drastic change in the peaks.

7.1. DSC Analysis of Clotrimazole:

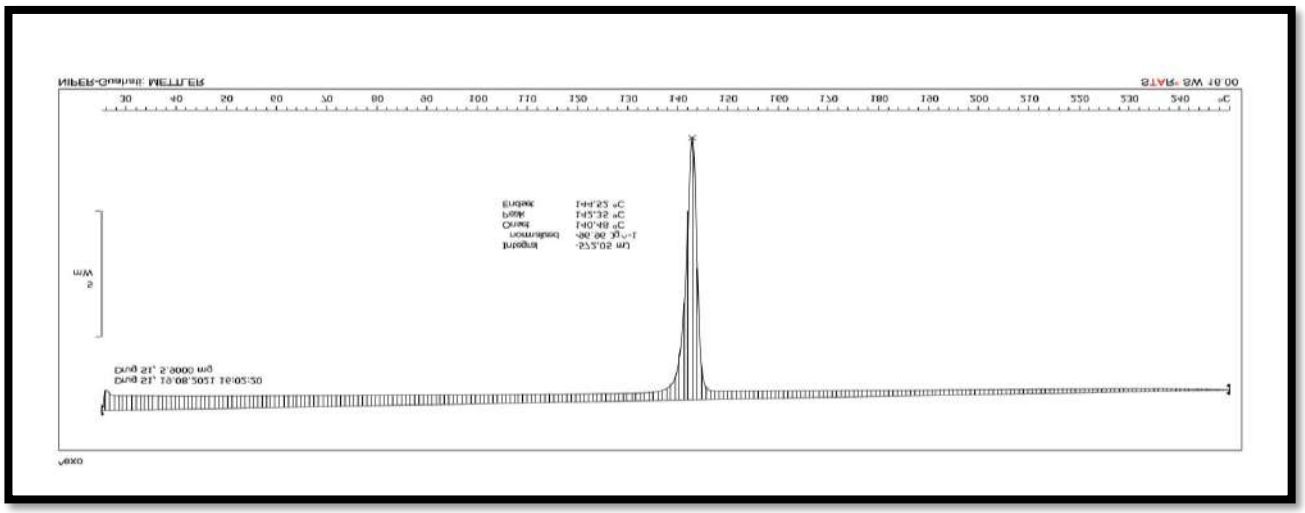
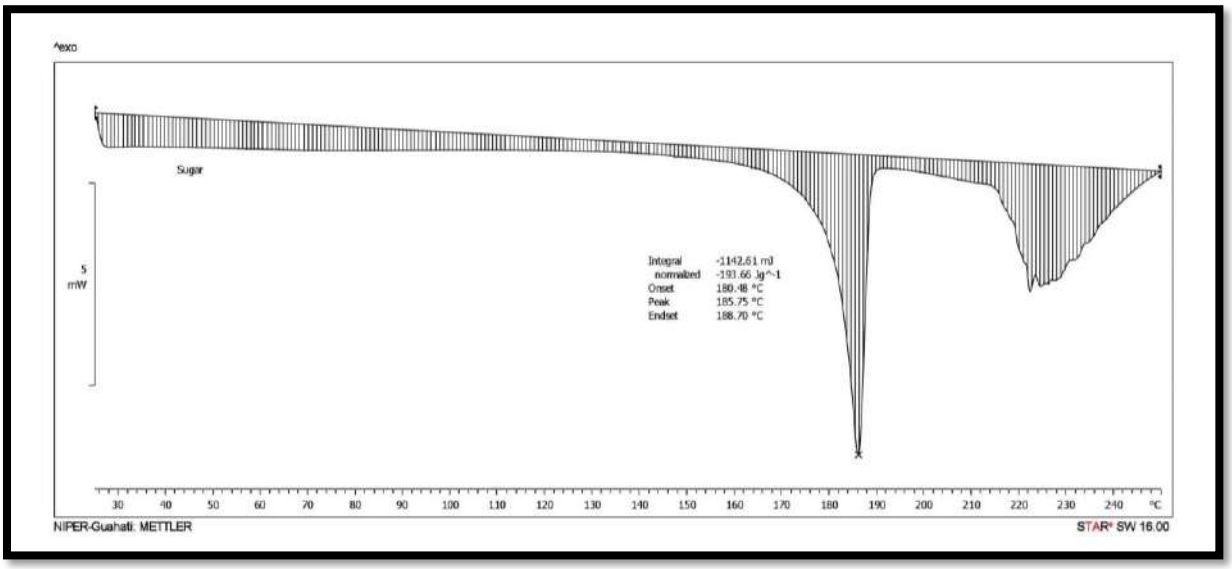


Fig 12: DSC of Clotrimazole.

CHAPTER 5- RESULT & DISCUSSION

7.2. DSC analysis of Palmyra Palm Sugar:

Fig 13: DSC of Palmyra Palm Sugar.



7.3. DSC of Solid Dispersion:

.

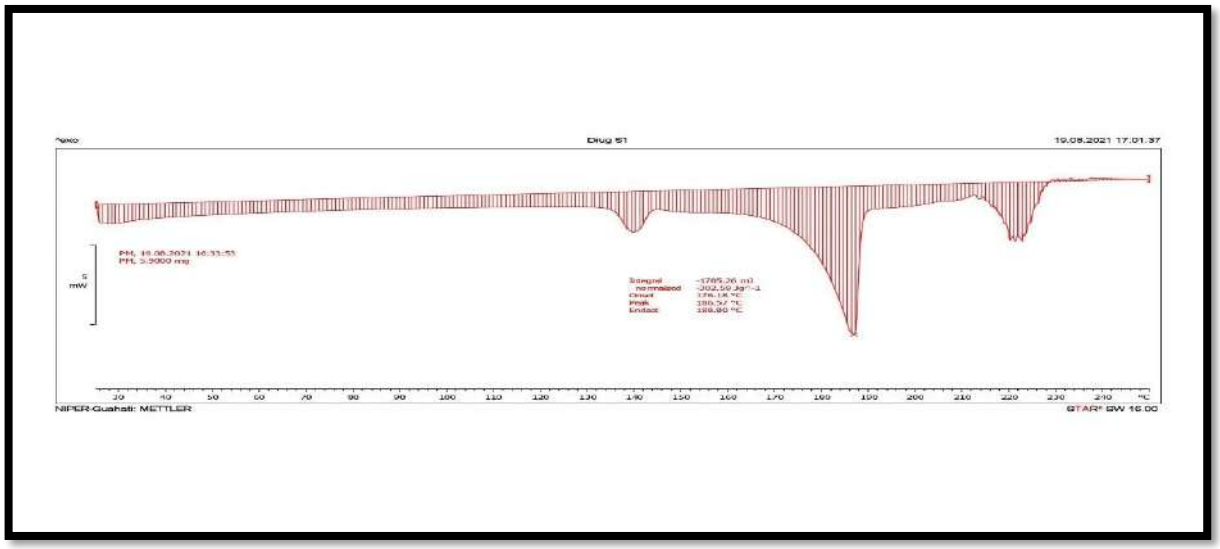


Fig 14: DSC analysis of Mixture of Palmyra Palm Sugar & Clotrimazole

7.4. Combined Graph of All the Samples:

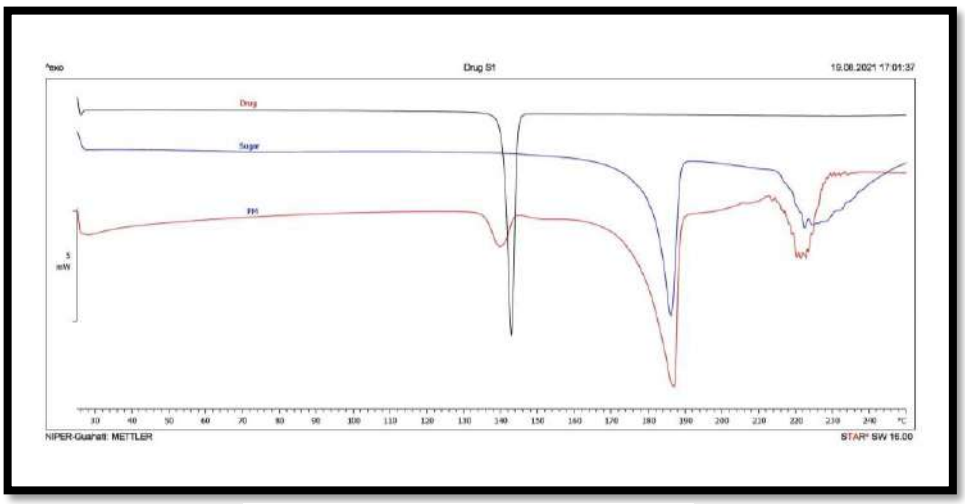


Fig 15: DSC Peaks of All the Samples.

PRE-COMPRESSION PARAMETERS:

Parameters	Results
Bulk density (gm/cm^3)	0.47
Tapped density (gm/cm^3)	0.57
Carr's Index	17.54
Hausner's Ratio	1.21
Angle of Repose	33.69
Porosity (%)	18

Table 14: Powder properties.

CHAPTER 5- RESULT & DISCUSSION

POST-COMPRESSION PARAMETERS:

1. All the formulation of clotrimazole prepared were evaluated for the following physical and organoleptic parameters:

1.1 Physical Parameters:

Size: Thickness is 4.504 mm & Diameter is 11. 518 mm.

Shape: Cylindrical Shape.

1.2 Organoleptic Parameters:

Colour: Pale white colour.

Taste: Tasteless.

Odour: Characteristics.

2. Tablet Properties:

2.1 Hardness test: Hardness test: Hardness of the tablets was measured by using Monsento Hardness tester. The avg. hardness of tablets was found to be 8.1 kg.

2.2 Friability test: Friability of the 10 tablets were measured using Roche Friabilator. This device subjects the tablets to the combined effect of abrasion and shock by using a plastic chamber that revolves at 25 rpm dropping the tablets from a distance of 6 inches with each revolution. The tablets were weighed before placing them in the friabilator & allow to rotate for 100 revolution and after that re-weighed. The friability was found to be 0.82%.

2.3 Weight variation test: 20 tablets were randomly selected and average weight was determined. Then individual tablets were weighed and percent deviation from the average was calculated. For the formulations weight variation is within the limit. The prepared tablets were found to be within the prescribed range.

Average weight of tablet(mg)	Percentage difference allowed
<130	10
130- 324	7.5
>324	5

Table 15: Weight variation standard table.

2.5 In vitro disintegration time: The time in seconds taken for complete disintegration of the tablet with no pulpable mass remaining in the apparatus was measured and recorded. The disintegration time was found to be 17.18 sec

2.6 In vitro dissolution studies:

It was studied by using USP type II apparatus at 50 rpm using 900 ml of 0.1N HCL (pH1.2) as dissolution medium. The temperature of the dissolution medium was maintained at 37±0.5-degree Celsius; 5ml of the sample from dissolution medium was withdrawn at every 5 min interval and filtered through Whatman filter paper. The absorbance of the sample was measured by UV spectrophotometric method at 264nm and cumulative % drug release was calculated by using an equation obtained from a standard calibration curve. After that Curve was plotted both of F_1 (Clotrimazole containing tablets) & F_2 (Solid Dispersion containing tablets).

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F_1:

Time (Min)	Absorbance	Conc. (µg/ml)	DF	Conc. (µg/ml)	Conc. (mg/ml)	Conc. 5ml (mg/ml)	Conc.900 ml(mg)	%Cumulative
0	0	0	10	0	0	0	0	0
5	0.0189	13.48	10	134.8	0.1348	0.674	606.6	5.38
10	0.0756	36.16	10	361.6	0.3616	1.808	1627.2	7.78
15	0.1256	56.16	10	561.6	0.5616	2.808	2527.2	17.01
20	0.1734	75.28	10	752.8	0.7528	3.764	3387.6	26.56
25	0.2345	97.92	10	979.2	0.9792	4.896	4406.4	35.08

F2.

Time (Min)	Absorbance	Conc. (µg/ml)	DF	Conc. (µg/ml)	Conc. (mg/ml)	Conc. 5ml(mg/ml)	Conc. 900ml(mg)	%Cumulative
0	0	0	10	0	0	0	0	0
5	0.031	18.32	10	183.2	0.1832	0.916	824.4	5.76
10	0.0926	42.96	10	429.6	0.4296	2.148	1933.2	8.01
15	0.1444	63.68	10	636.8	0.6368	3.184	2865.5	12.51
20	0.1933	83.24	10	832.4	0.8324	4.162	3745.8	21.51
25	0.2598	109.84	10	1098.4	1.0984	5.492	4942.8	39.51

Table 16: Cumulative dissolution of Clotrimazole (F_1) & Solid Dispersion (F_2) containing tablets.

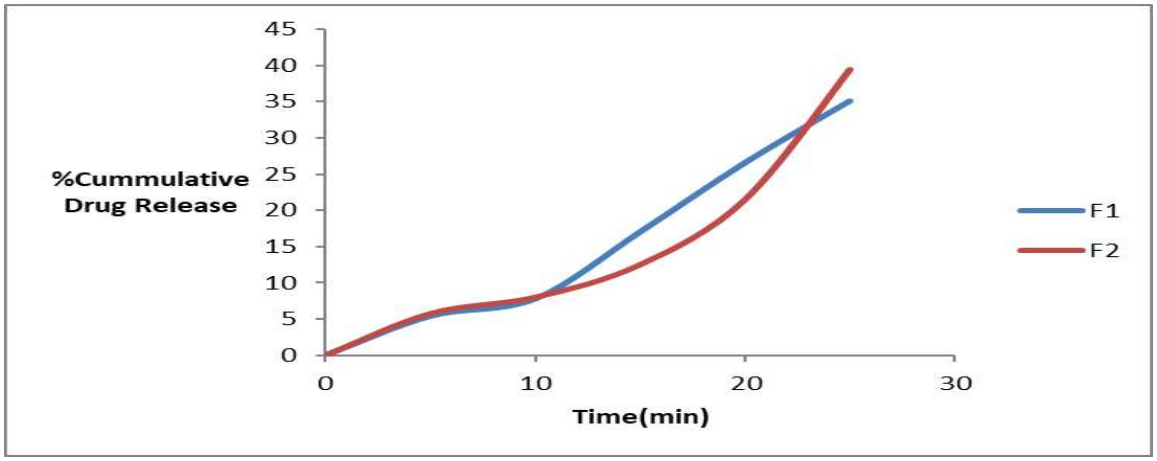

Fig 16: Time Vs Cumulative Release Curve of both F_1 & F_2

CHAPTER 5- RESULT & DISCUSSION

CHAPTER 7- SUMMARY

SUMMERY – FORMULATION AND EVALUATION OF CLOTRIMAZOLE SOLID DISPERSION FAST DISINTEGRATING TABLETS USING PALM SUGAR (*TAL MISHRI*).

This thesis deals with the background investigation on the drug Clotrimazole its advantage and disadvantage and its recent uses. The chapter also through light on a brief study on solid dispersion its types, a brief study on solid dosage forms its application its advantage and disadvantage. This chapter also contains a brief study of fast disintegrating tablets, challenges in the preparation of fast disintegrating tablets. Here also discussed about Palmyra Palm Sugar. Then it deals with the literature review on previous similar. It also signifies the major aim, objective and rational of the work. The plan of work carried out for completing the project work, is also described here properly. The material and methodology for the formulation and evaluation of different parameter of tablets, evaluating drug excipients interaction studies is also described here, the results and discussion of preparation and evaluation of Clotrimazole & Palmyra Palm Sugar solid dispersion fast disintegrating tablets.

CHAPTER 8- CONCLUSION

CONCLUSION

Clotrimazole is an anti-fungal drug. In biopharmaceutical classification system clotrimazole comes in BCS class 2 category. Being a BCS class II drug, it is very poorly soluble in water, which results in the slow dissolution and hence low bioavailability when administered orally. Oral bioavailability of a drug depends on its solubility and/or dissolution rate, therefore efforts to increase dissolution of drugs with limited water solubility is often needed. So, in the present study solid dispersion approach with Palmyra Palm Sugar used in the improvement of solubility of clotrimazole. Because Several drugs have been shown to exhibit better aqueous solubility and dissolution characteristics in the form of Solid dispersion with other type of sugars also. To overcome the low bioavailability, solid dispersion technique used to increase the bioavailability of clotrimazole, and in the fast-disintegrating tablets Solid Dispersion of Clotrimazole & Palmyra Palm Sugar was used. As we can see in evaluation studies that both clotrimazole and palmyra palm sugars are very much compatible with each other, so this can also have a future aspect of being used in many other formulations also, but for until now the FST prepared with clotrimazole solid dispersion with palm sugar has shown quite remarkable results, in the In-Vitro dissolution studies, which was done to measure the cumulative drug release. So, in future Palmyra Palm sugar which have been used as an excipient in for solid dispersion, can also be used in other BCS-II classification drugs also.

CHAPTER 9- REFERENCES

REFERENCES

1. Sameer G, Late, Yi-Ying Yu, Ajay K. Effect of disintegration- promoting agent, lubricants and moisture treatment on optimized fast disintegrating agent. Int J Pharm. 2008:1-8.

2. Chien YW. Novel drug delivery systems. New York – Marcel Dekker Inc., 2nd ed. 1992.

3. Abdelbary G, Prinderre P, Eouani C, Joachim J, Reynier.J.P. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. In t j pharm. 2004; 278: 423-33.

4. Gohel M, Patel M, Amin A, Nehal BA. Formulation design and optimization of mouth dissolving tablets of nimesulide using vacuum drying technique. AAPS Pharm Sci-Tech. 2004;5(3): 1-6.

5. Schiermeier S, Schmidt PC. Fast dispersible ibuprofen tablets. Eur j Pharm Sci. 2002: 295-305

6. Bandari S, Mittapalli RK, Gannu R, Rao MY. Orodispersible tablets: Anoverview. Asian JPharm. 2008: 2-11.

8. Mishra B, Shukla D, Chakraborty S, Singh S, Mouth Dissolving Tablets I: An Overview ofFormulation Technology, Scientia Pharmaceutica, 2009, 77, 309–326.

9 Sreenivas SA, Dandagi PM, Gadad AP, Indian Journal of Pharmaceutical Education andResearch, 2005, 39(4), 177-181.

10. Bandari S, Mittapalli RK, Gannu R, Asian Journal of Pharmaceutics, 2008, 2(1), 2-11.

11. Kuchekar BS, Bhise SB, Arumugam V, Indian Journal of Pharmaceutical Education, 2001,35(4), 150-152.

12. Reddy LH, Ghosh BR, Fast dissolving drug delivery systems: A review of the literature, Indian Journal of Pharmaceutical Sciences, 2002, 64(4), 331-336.

13. Bhandari S, Mittapalli RK, Gannu R, Rao YM, Orodispersible tablet: An overview, AsianJournal of Pharmaceutics, 2008, 2-10.

14. Hirani JJ, Rathod DA, Vadalia KR, Orally Disintegrating Tablets: A

15. Review, Tropical Journal of Pharmaceutical Research, 2009, 8 (2), 161-172

16. Brown D, orally disintegrating tablets: Taste over speed, Drug Delivery Technology, 2001, 3 (6), 58-61.

17. Seager H, Drug-delivery products and Zydis Fast-dissolving dosage form, Journal of Pharmacy and Pharmacology, 1998, 50, 375-382.

18. Lies MC, Atherton AD, Copping NM. Freeze-dried dosage forms and methods for preparing same. US Patent 5,188,825 (1993).

19. Habib W, Khankari R, Honts J, Fast dissolving drug delivery systems, Critical Reviews in Therapeutic Drug Carrier Systems, 2000, 17(1), 61-72. 24. Ghosh TK, Chatterjee DJ, Pfister WR, Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and biopharmaceutical perspective. In: Ghosh TK and Pfister WR (Eds). Drug Delivery to the Oral Cavity: Molecules to

Market. NY, USA: CRC Press, 2005, pp 337-356. 25. Sugihara M, Hidaka M, Saitou A, Discriminatory features of dosage form and package, Japanese Journal of Hospital Pharmacy, 1986, 12, 322-328.

20. Ghosh TK, Chatterjee DJ, Pfister WR, Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and biopharmaceutical perspective. In: Ghosh TK and Pfister WR (Eds). Drug Delivery to the Oral Cavity: Molecules to Market. NY, USA: CRC Press, 2005, pp 337-356.

21. Sugihara M, Hidaka M, Saitou A, Discriminatory features of dosage form and package, Japanese Journal of Hospital Pharmacy, 1986, 12, 322-328.

22. Dharna Allawadi*, Neelam Singh, Sukhbir Singh and Sandeep Arora. Solid dispersion a review on drug dlivery system and solubility enhamcement. IJPSR, 2013; Vol. 4(6): 2094- 2105.

23. Patidar K, Kshirsagar MD, Saini V, Joshi PB and Soni M: Solid Dispersion Technology: A Boon for Poor Water-Soluble Drugs. Indian Journal of Novel Drug Delivery 2011; 3(2): 83- 90.

24. Hasegawa S: Effects of water content in physical mixture and heating temperature on crystallinity of troglitazone-PVP K30 solid dispersions prepared by closed melting method. International Journal of Pharmaceutics 2003; 302(29): 103– 112.

25. Rodier E: A three step supercritical process to improve the dissolution rate ofEflucimibe. European Journal of Pharmaceutical Sciences 2005; 26: 184–193.

26. Goldberg A, Gibaldi M and Kanig L: Increasing dissolution rates and gastrointestinal

absorption of drugs via solid solutions and eutectic mixtures II experimental evaluation of a eutectic mixture: urea-acetaminophen system. Journal of Pharmaceutical Sciences 1996; 55: 482-487.

27. Mooter G: Evaluation of Inutec SP1 as a new carrier in the formulation of solid dispersions for poorly soluble drugs. International Journal of Pharmaceutics 2006; 316: 1–6.

28. Chauhan B: Preparation and evaluation of glibenclamide polyglycolized glycerides solid dispersions with silicon dioxide by spray drying technique. European Journal of Pharmaceutical Sciences 2005; 26: 219–230.

29. Mizuno M: Inhibition of a solid phase reaction among excipients that accelerates drug release from a solid dispersion with aging. International Journal of Pharmaceutics 2005; 305: 37–51.

30. Drooge, DJV: Characterization of the Mode of Incorporation of Lipophilic Compounds in Solid Dispersions at the Nanoscale Using Fluorescence Resonance Energy Transfer (FRET). Macromolecular Rapid Communications 2006; 27: 1149–1155.

31. Eriksson HJC, Hinrichs WLJ, Veen B, Somsen GW, Jong GJ and Frijlink HW: Investigations into the stabilisation of drugs by sugar glasses: I, Tablets prepared from stabilised alkaline phosphatise. International Journal of Pharmaceutics 2002; 249(1-2): 59-70.

32. Sethia S and Squillante E: Solid dispersions: revival with greater possibilities and applications in oral drug delivery. Critical Reviews of Therapeutic Drug Carrier System 2003; 20(2-3): 215-247.

33. 32. Huang J: Nifedipine solid dispersion in microparticles of ammonio methacrylate

copolymer and ethylcellulose binary blend for controlled drug delivery: Effect of drug loading on release kinetics. International Journal of Pharmaceutics 2006; 319: 44–54.

34. Srikaeo K, Likittrakulwong W. Productions and Functional Properties of Palm Sugars 1) Molecular Immunology of Potentially Immune-rlated Genes for Therapeutic Strategy Development Applicable in Aquaculture 2) Breeding Programs for Discovery of Disease Resistance in Economically Aquatic Species View Project Germinated Paddy Rice View project. 2019; Available from: http://wjst.wu.ac.th.

35. Ishak MR, Sapuan SM, Leman Z, Rahman MZA, Anwar UMK, Siregar JP. Sugar palm (Arenga pinnata): Its fibres, polymers and composites. Vol. 91, Carbohydrate Polymers. 2013. p. 699–710.

36. Arulandoo X, Sritharan K, Subramaniam M. The Coconut Palm. In: Encyclopaedia of Applied Plant Sciences. Elsevier Inc.; 2016. p. 426–30.

37. Sahu O. Assessment of sugarcane industry: Suitability for production, consumption, and utilization. Annals of Agrarian Science [Internet]. 2018;16(4):389–95. Available from: https://doi.org/10.1016/j.aasci.2018.08.001.

38. Tsang WSC, Clarke MA. Chemistry of Sugar in Food Processing [Internet]. Vol. 9, Sugar Series. Elsevier B.V.; 1988. 292–302. Available from: http://dx.doi.org/10.1016/B978-0-444-43020-5.50024-2

39. Polynesian M, Arabs T, Crusaders T, Indies W, World N, Pyramid G, et al. 7 Sugars. 1997.

40. . Madgulkar A, *et al;* Sugars as solid dispersion carrier to improve solubility and dissolution of the BCS class II drug: clotrimazole; Drug Development Industrial Pharmacy; 42(1), 28-38; 15 April 2015.

41. Surendra S; Formulation, Evaluation & Optimization of Clotrimazole Solid dispersion incorporated gels; International Journal of PharmTech Research 3(3):1345-1354; July 2013.

42. Balata G, Mahdi M, Bakera R. Improvement of solubility and dissolution properties of clotrimazole by solid dispersion and inclusion complexes. Ind J Pharm Sci 2013; 73:517–26.

43. Srikaeo K, Likittrakulwong W. Productions and Functional Properties of Palm Sugars 1) Molecular Immunology of Potentially Immune-rlated Genes for Therapeutic Strategy Development Applicable in Aquaculture 2) Breeding Programs for Discovery of Disease Resistance in Economically Aquatic Species View Project Germinated Paddy Rice View project. 2019; Available from: http://wjst.wu.ac.th.

44. Das, A., Nayak, A. K., Mohanty, B., & Panda, S. (2011). Solubility and Dissolution Enhancement of Etoricoxib by Solid Dispersion Technique Using Sugar Carriers. *ISRN Pharmaceutics*, *2011*(Peg 4000), 1–8. https://doi.org/10.5402/2011/819765.

45. van der Merwe J, Steenekamp J, Steyn D, Hamman J. The role of functional excipients in solid oral dosage forms to overcome poor drug dissolution and bioavailability. Pharmaceutics. 2020;12(5).

46. Saputro AD, van de Walle D, Dewettinck K. Palm Sap Sugar: A Review. Vol. 21, Sugar Tech. Springer; 2019. p. 862–7.

47. Gardner E. Coconut sugar. Vol. 223, British Dental Journal. Nature Publishing Group; 2017. p. 749.

48. Ngwuluka NC, Idiakhoa BA, Nep EI, Ogaji I, Okafor IS. Formulation and evaluation of paracetamol tablets manufactured using the dried fruit of Phoenix dactylifera Linn as an

excipient. Research In Pharmaceutical Biotechnology [Internet]. 2010;2(3):25–32. Available from: http://www.academicjournals.org/RPB.

49. Al-Remawi M, Elsayed A, Maghrabi I, Hamaidi M, Jaber N. A novel pharmaceutical excipient: Coprecipitation of calcium and magnesium silicate using brine-seawater in date palm cellulose as an absorbing host. Journal of Excipients and Food Chemicals. 2017;8(3):62–74.

50. Sahari J, Sapuan SM, Zainudin ES, Maleque MA. Sugar palm tree: A versatile plant and novel source for biofibres, biomatrices, and biocomposites. Polymers from Renewable Resources. 2012;3(2):61–78.

51. Walsh J, Cram A, Woertz K, Breitkreutz J, Winzenburg G, Turner R, et al. Playing hide and seek with poorly tasting paediatric medicines: Do not forget the excipients. Advanced Drug Delivery Reviews [Internet]. 2014; 73:14–33. Available from: http://dx.doi.org/10.1016/j.addr.2014.02.012

52. Sopyan I, Widya Sukma Santi NM, Virisy Berlian A, Erin Meilina N, Fauza Q, Amelia Apriyandi R. A review: Pharmaceutical excipients of solid dosage forms and characterizations. International Journal of Research in Pharmaceutical Sciences. 2020;11(2):1472–80.

53. Yohana Chaerunisaa A, Sriwidodo S, Abdassah M. Microcrystalline Cellulose as Pharmaceutical Excipient. Pharmaceutical Formulation Design - Recent Practices. 2020.

54. Builders PF, Arhewoh MI. Pharmaceutical applications of native starch in conventional drug delivery. Starch/Staerke. 2016;68(9–10):864–73.

55. 1. ChPrabhakar, Balakrishna K. A Review on Nanosuspensions in Drug Delivery. Int J of Pharm Bio Sci 2011; 2(1):549-558.

56. 2. Shid L R,Dhole N S, Kulkarni N, Shid L S. Nanosuspension: A review.IntJPharm Sci Rev Res 2012;1(22): 98-106.

57. Lakshmi P, GiddamA K. Nanosuspension Technology: A review.IntJ Pharm PharmSci 2010; 2(4):35-40.

58. Patel M, Shah A, Patel N M. Nanosuspension: A Novel Approach for Drug Delivery System. J Pharm Sci Biores 2011; 1(1):1-10.

59. Rane R D, Gulve N H, Patil V.V. formulation and evaluation of fast dissolving tablet of albendazole. IntCurr Pharm J 2012; 1(10):311-316.

60. Madgulkar, Ashwini, et al. "Sugars as Solid Dispersion Carrier to Improve Solubility and Dissolution of the BCS Class II Drug: Clotrimazole." *Drug Development and Industrial Pharmacy*, vol. 42, no. 1, 2015, pp. 28–38., doi:10.3109/03639045.2015.1024683.

61. Sharma, Deepak. "Fast Disintegrating Tablets: A Review on An Emerging Trend in Novel Oral Drug Delivery Technology and New Market Opportunities." Journal of Drug Delivery and Therapeutics, vol. 2, no. 3, 2012, doi:10.22270/jddt. v2i3.125.

62. Subramanyan CVS. Text book of Physical Pharmaceutics. 1st Edn., Published by Vallabh Prakash. P. No.223.

63. Alfred Martin. Text book of Physical Pharmacy 4th Edn., B.I Wavesly Pvt Lts. P.No. 443.

64. Bhagwati ST, Hiremath SN, Srinivas SA. Comparative Evaluation of disintegrants by formulating Cefixime dispersible tablets. Indian Journal of Pharmaceutical Education; 2005 Oct-Dec., 39(4); 194.

65. 11. Kuchekar BS, Badhan AC, Mahajan HS. Mouth Dissolving tablets of Salbutamol Sulphate. A Novel drug delivery system. Indian Drugs 2004 Oct, 41(10): 592-594.

CHAPTER 9- LIST OF PAPERS

LIST OF PAPERS

LIST OF PAPERS PUBLISHED:

- **Bordoloi SS**, Chakraborty T, Das A, Islam J, Rynjah D and Baishya B.: The Applicability of Palm Trees in Pharmaceuticals as Excipients with a special emphasis on Palm Sugar: A Review. World Journal of Pharmaceutical Research. 2021; 10(6): 1778-1792.
- **Rynjah D**, Chakraborty T, Das A, Islam J, Bordoloi SS, Baishya B and Hasan N.: Recent development in the formulations of ginger for therapeutic applications and an over view towards the action on SARS-COV-2. Int J Pharm Sci & Res 2021; 12(7): 3537-48.
- **Islam J**, Chakraborty T, Das A, Rynjah D, Bordoloi SS, and Baishya B.: The wound Healing activity of *Calendula officinalis*: A Review. World Journal of Pharmacy and Pharmaceutical Sciences. 2021; 10(7): 512-523.
- **Baishya B,** Rahman SS, Rynjah D, Bordoloi SS, Islam J and Hasan N.: Enhancing of Oral Bioavailability of Poorly water-soluble antihypertensive drugs. International Journal of Current Pharmaceutical Research. 2021; 13(4): 42-47.

THE APPLICABILITY OF PALM TREES IN PHARMACEUTICALS AS EXCIPIENTS WITH A SPECIAL EMPHASIS ON PALM SUGAR: A REVIEW.

***Saranga Shekhar Bordoloi, Tapash Chakraborty, Asha Das, Jakirul Islam, Damanbhalang Rynjah and Bitopan Baishya.**

Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hatkhowapara, Azara, Guwahati-781017, Assam, India.

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***Corresponding Author**
Saranga Shekhar Bordoloi
Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hatkhowapara, Azara, Guwahati-781017, Assam, India.

ABSTRACT

Palms like Sugar palm, palmyra palm tree, date tree, coconut palm, raphia palm, oil palm, sago palm & nypa palm fall under the family of Arecaceae, which are well known for their sweet sap from where we get sugar. Sugar from palm is generally used locally in desserts as a sweetener. Generally, this sugar is consisting of significant amount of fructose & glucose rather than only sucrose, but still, the major palm sugar content is sucrose. Sugar obtained from palm has also been seen to having less GI (Glycaemic index) value compare to cane sugar, so this sugar has great health benefits. Many Palm products including sugar, are used in pharmaceuticals as excipients. Palm has been seen to be used as binder, starch source, oil, bioethanol, gums, super- disintegrants, nanocrystalline cellulose, microcrystalline cellulose, masking agent, etc. As we found that sugar is highly soluble in water, it can be used to form a solid solution with BCS-II classification drugs to increase the bioavailability of the drug as we know aqueous solubility is directly proportional to bioavailability. So, we can also use Palm sugar for this purpose.

KEYWORDS: Palm, Palm sap, Palm sugar, Palm sugar content, Palm excipients.

INTRODUCTION

The excipients of natural sources have countless benefits compare to their synthetic equivalents