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MEDICATED CHOCOLATE: A NOVEL SOLID DOSAGE FORM

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ABSTRACT

Chocolate is highly sophisticated a versatile food that can be used to create a wide variety of taste and texture experiences. Additionally, because chocolate is an anhydrous medium, it resists the growth of microorganisms and the hydrolysis of active ingredients that are sensitive to water. Sweetening, flavoring, and coloring agents are added to medicated chocolate in order to make it attractive to pediatric patients. The benefits of medicated chocolate include masking the taste of bitter medications, improving bioavailability, and lengthening the dosage form duration in the oral cavity, which also reduces gastric irritation. Chocolate is one of the most widely consumed foods in the world due to its high nutritional content, quick metabolism, and excellent digestion. In many ways, chocolate is an excellent medium for delivering active ingredients. Medicated chocolate formulations are commonly used for pediatric administration, and they increase the patient compliance to consume the medication. Because conventional dosage forms, such as tablets and capsules, have certain limitations when it comes to pediatric patients for instance, the bitterness of the tablet and their inability to swallow it. Medicinal chocolate is a more acceptable dosage form in pediatrics. Patients with diabetes can also benefit from the chocolate drug delivery system provided by dark chocolate-containing medications. The medicated chocolate can be evaluated for its appearance, moisture content, viscosity, blooming test, drug content determination and in vitro drug release. Medicated chocolate is prepared by using chocolate base and drug is incorporated to prepared chocolate base.

KEYWORDS: Medicated chocolate, patient compliance, pediatric patient, chocolate.

INTRODUCTION

The development of pediatric formulations can present significant scientific challenges because of their specific requirements and limitations. The diversity of children, taste masking, physical, chemical, and microbiological stability, achieving worldwide regulatory acceptability, expedited development timelines, and providing rapid patient access are some of the challenges associated with developing pediatric formulations. Oral drug delivery optimization has been one of pediatric pharmacology's biggest problems. Tablet crushing may alter the bioavailability of a drug by affecting the rate or degree of absorption. Another common practice is cutting tablets; this can introduce significant variability between doses, but it may be acceptable for some drugs. An imprompt oral suspension or solution may also have problems with handling, adding flavoring, switching brands, or stabilizing the finished product. It may also affect the drug's absorption properties. While commercially available oral liquid medications offer infants and children a more dependable, ready-to-use preparation, bioequivalency with solid oral dosage forms is still not guaranteed. The issues with the formulations currently on the market emphasize the need for the creation of novel products with improved taste, consistency in serum drug concentrations, and ease of administration.[1]

Chocolate is an highly sophisticated and adaptable food that can be used to create a wide variety of taste and texture experiences. Additionally, because chocolate is an anhydrous medium, it resists the growth of microorganisms and the hydrolysis of active ingredients that are sensitive to water. In many ways, chocolate is an excellent medium for delivering active ingredients. For instance, chocolate's organoleptic properties are great at hiding the off-putting flavors of some active ingredients and giving otherwise unappealingly gritty active agent compositions a smooth, creamy texture.

Compounds like methyl xanthines, di and tri terpenes, polyphenols, saturated fat, and sterols are all abundant in chocolate.

The main component of chocolate is cocoa, which has a high polyphenol content, especially in flavan-3-ols like procyanidins, epicatechins, and catechins. Studies indicate that eating a lot of flavonoids, a type of polyphenol, in your diet, such as chocolate, may lower your risk of heart attack in the chest. The protective effect could be partially explained by flavonoids' antioxidant properties.[1,2]

Utilizing chocolate base, the medication is mixed into the finished product to create medicated chocolate. The drug delivery system known as "chocolate" offers benefits such as the potential to avoid pre-systemic elimination in the GI tract and to circumvent the first-pass effect as the drug is incorporated into and released from the chocolate. Due to its anhydrous nature, chocolate is also resistant to microbiological growth and the hydrolysis of active ingredients that are sensitive to water. In many ways, chocolate is an excellent medium for delivering active ingredients. Dark chocolate, also referred to as black chocolate or plain chocolate, is made by combining sugar and cocoa powder; the resulting product has a higher cocoa content.[3]

History of Chocolate

Chocolate originated from Mexico where the Mayas, Incas and Aztecs cultivated the cocoa tree. It was initially thought to be an aphrodisiac available only to the wealthy and well-off. Coffee and tea took the place of chocolate as the primary beverage due to its high cost. Cocoa is now mostly grown in Sri Lanka, Indonesia, and West Africa. The cocoa tree's scientific name, theobroma cocoa, originates from the Greek words theo, which means god, and broma, which means drink. Swedish naturalist Carl Von Linne gave this association to the tree (1707-1778). The social, religious, and economic significance of chocolate in both old and new world cultures is actually symbolized by this name.[3]

TYPES OF CHOCOLATE

1. Milk chocolate

It is recommended to use Ecuadorian beans along with mostly medium-roasted West African beans. A nice, clean cocoa with nutty and faintly fruity undertones would be produced by this blend. It's crucial to remember that adding the extremely acidic Brazilian and Malaysian beans would ruin the intended milky notes.

2. Light milk chocolate

Lightly roasted Java beans, which have a light color and a very mild flavor with nutty overtones, can be used to make this product. This would make the coating several shades lighter than a 100% West African bean, which would help achieve a good standard of identity for milk chocolate.

3. Dark chocolate

They are also known as “plain chocolate” and “black chocolate”, is produced using high percentages of cocoa. Dark chocolate is mostly eaten as it is. Usually, it contains high cocoa; percentages ranging from 70% to 99% are sold. The dark chocolate contains higher antioxidants, such as polyphenols, as and is relatively less in sugar.[4]

4. Semisweet chocolate

To enhance desired notes and minimize burnt/bitter notes, use mostly West African stock, which has a cocoa character and slightly nutty undertones (light to medium roast). Caracas and Trinidad beans would enhance this blend with floral and mildly spicy notes to produce a well-balanced but distinctive profile.

5. Bittersweet chocolate

Because it yields extremely bitter coatings, this product is primarily intended for use on extremely sweet and highly flavorful cream centers. “Bittersweet chocolate” is chocolate liquor to which some sugar, more cocoa butter, vanilla flavoring, and sometimes lecithin has been added. It usually has inadequate sugar more liquor than semisweet chocolate. Bittersweet and semisweet chocolate are sometimes referred to as “couverture “(chocolate that contains at least 32% cocoa butter). In those types of chocolate, higher the percentages of cocoa and it are less sweet the chocolate.

6. Semisweet cookie drop

To achieve a good cocoa impact, it is recommended that this product use the dominant West African beans. The West African component is contrasted and complemented by the powerful profiles of the Sanchez and Brazilian components. In this application, a robust flavour is desirable for contrast in the baked cookie.

7. Cocoa powder

The majority of the time, baking calls for "cocoa powder." that is also used for beverages that have sugar and milk added. Unsweetened cocoa powder comes in two varieties: a natural variety (similar to short the produce by the broma process) and a Dutch-process variety. The bulk of the flavonoids found in cocoa were divided during the Dutch processing. Hershey discontinued producing pure European-style cocoa using the Dutch process in 2005 and switched to a special dark blend of natural and Dutch-process cocoa.[5]

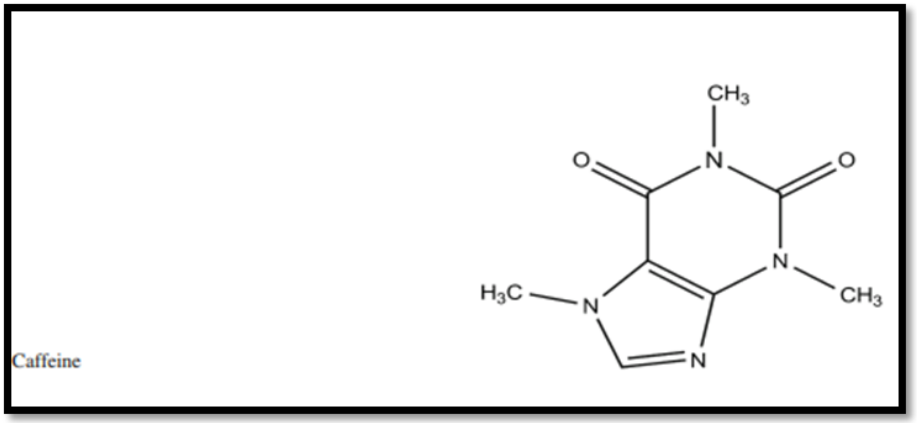
Physical Properties of Chocolate

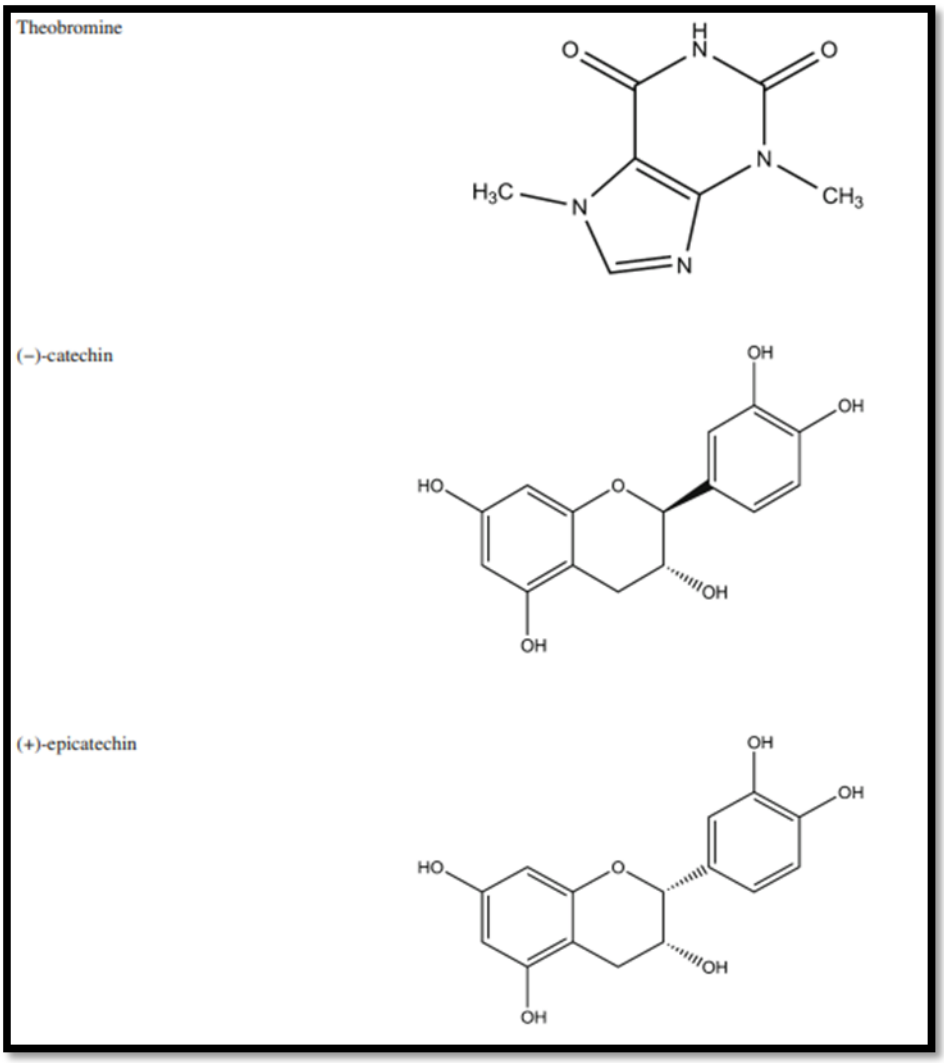
- The most popular types of chocolate are cocoa powder and butter. The melting point of cocoa is approximately 34–30°C (93–101°F).
- Rendering room temperature solid chocolate that easily melts in the mouth.
- Cocoa butter exhibits polymorphism; α has a melting point of 17°C, γ has a melting point of 23°C, β has a melting point of 26°C, and the β crystal has a melting point of 35–37°C. Because of its high melting point, β-crystal form is commonly used in the production of chocolate. A homogeneous crystal structure will yield a glossy, snappy, and smooth texture.
- When cocoa butter's temperature rises, its structure takes on a less stable form that melts below room temperature. Chocolate is most stable when it is in the β crystal form.

- The advantages are taken of this phenomenon in the polymorphic transformation theory of chocolate bloom.
- Cocoa butter's refractive index ranges from 1.44556 to 1.44573.
- Cocoa butter has an iodine value ranging from 32.11 to 35.12.35.57.
- Cocoa butter has an acid value of 1.68 and a saponification value of 191.214, 192.88 to 196.29.
- The color of natural cocoa powder is light brown, and its extractable pH ranges from 3.5 to 5.8.
- The processed (alkalized) cocoa powder has a pH of 6.8 to 8.1 and a deeper color that ranges from brownish red to almost black.[6]

CHEMISTRY

- Commercial theobromine is made from the husks of cocoa beans. Triglyceride fatty acids, which are mostly composed of oleic, stearic, and palmitic acids, are found in cocoa butter.
- Alkaloids, theobromine (0.5%) to 2.7%, amines, theophylline, caffeine (about 0.25% in cocoa), fatty acids, triamine, trigonelline, magnesium, polyphenols (including flavoring), phenythyamine, and n-acyl ethanolamines are among the pharmacologically active components of cocoa seeds. been discovered).
- Theobromine (86–240 mg) and caffeine (9–31 mg) are present in a typical chocolate bar (40–50 g). When cocoa is roasted, the reaction between diketopiperazines and theobromine produces the distinctively bitter flavor.
- Myristic, arachidic, lauric, palmitic, linoleic, and α linolenic acids are also present in it. Polyphenols found in cocoa are rich and can help prevent cardiovascular disease.
- By weight, cocoa contains over 10% flavanol. In cocoa beans, flavanols can be polymeric (composed of a combination of monomers and chains of up to 10 units or more) or dimeric (composed of two units of epicatechin with different linkages). Monomeric flavanols are primarily (-)-epicatechin and (+) catechin.
- Theophylline, alkaloids, theobromine (0.5%) to 2.7%, amines, caffeine (approximately 0.25% in cocoa), fatty acids, and theophylline are among the pharmacologically active components of cocoa seeds.acids, n-acyl ethanolamines, magnesium, polyphenols (including flavoring), triamine, trigonelline, and phenythyamine.[7-8]





MECHANISM

Cocoa has been reported to be a source of natural antioxidants, the free radical scavengers that preserve cell membranes, protect DNA, prevent the oxidation of lowdensity lipoprotein (LDL) cholesterol that leads to atherosclerosis and prevent plaque formation in arterial walls.

Catechins are phytochemical compounds found in high concentrations in a variety of plant-based foods and baverages. The catechin content in dark chocolate is 12 mg/100 gm. The epicatechin content in dark chocolate is 41.5 mg/100 gm. The consumption of catechins has been associated with a variety of beneficial effects including increased plasma antioxidant activity, bronchial artery dilation, fat oxidation and resistance of LDL to oxidation15. Epicatechin seems to be a major bioactive constituent of cocoa and other flavonol-rich foods and baverages16. It has been shown to improve endothelial function in animals and humans17. The antioxidant activity of cocoa has been attributed to the procyanidins and their monomeric precursors, epicatechin and catechin, which inhibit oxidation of LDL14. Dark chocolate and cocoa inhibit LDL oxidation and increase high-density lipoprotein (HDL)-cholesterol concentrations. Catechin and Epicatechin has been found in cocoa. In saltsensitive animal models of hypertension, epicatechin lowers blood pressure and the associated end-organ damage. Nitric oxide seems to play a key role in the protection of both hypertension and endothelial dysfunction. The antioxidant capacity of dark chocolate is 13.1/ 100 g.[9]

BENEFITS OF CHOCOLATE

- **Maintaining blood pressure and blood glucose level:** A study published in 2015 concluded that dark chocolates not only decreased the blood pressure, but also decreased the blood glucose level i.e. fasting blood sugar.
- **For the blood sugar:** dark chocolate helps blood vessels healthy and circulation unimpaired to protect against type II diabetes. The flavonoids in dark chocolate also help to reduce insulin resistance by helping cells to function normally and region the ability to used body's insulin efficiently. Dark chocolate also has a low glycemic index and it won't cause huge spikes in sugar levels.[10]
- **Antioxidant:** By administration of chocolates neutralizes the free radicals and protects the damage of body. The antioxidant property is due to highest content of polyphenols and flavonoids, present highly in dark chocolates.[11]
- **For cardiovascular disease:** research suggests that the chocolate, cocoa and flavan-3-ols are used for the prevention of cardiovascular disease. Consumption of foods rich in flavanols is also associated with improved cardiovascular outcomes, suggesting that this specific group of flavonoid may have potent cardio protective qualities. Dark chocolate may reduce the risk of atherosclerosis by thickening and hardening of the arteries and by restoring flexibility of the arteries and preventing white blood cells from sticking to the

blood vessel walls. The possible mechanism of this flavonoid may include reducing the oxidative stress, increasing the endothelial prostacyclin release, enhancing the endothelial function, increasing the sensitivity of insulin receptors, inhibiting the lipid oxidation and inhibiting the angiotensin converting enzyme.[12]

- **Prevention of cancer:** It is unbelievable but according to American Cancer Institute: 'The chocolates rich in flavonoids, researchers have also investigated whether it may play a role in cancer prevention. The studies of cancer prevention are still emerging.
- **Vasodilation:** Theobromine present helps in dilating the narrowed blood vessels and improves the blood flow and hence useful in reducing blood pressure.
- **For the cardio metabolic disorder:** In general, the cardio metabolic disorder exerts a burden on people. However, these are largely preventable. By systematic review and meta-analysis, the cocoa product containing flavanols have a potential to prevent cardio metabolic disorder.[13]
- **Diuretic action:** Theobromine acts as an diuretic ie. It helps in removing excess water by urination from the internal to external environment.
- **In magnesium deficiency:** In rats, the magnesium contained in cocoa has been show to prevent and correct chronic magnesium deficiency. Low intakes of magnesium may be responsible for some cardiovascular alteration as well as renal, GI, neurological and muscular disorder. The use of cocoa to treat or prevent magnesium deficiency in human has not been explored.[14]
- **Muscle relaxation:** Theobromine has its muscle relaxant property on cardiac tissues.
- **Action against tooth decay:** Theobromine acts against the micro-organisms in the buccal cavity as thereby contributes to prevent the teeth from decaying.[15]
- **Antidepressant action:** Administration of chocolates leads to stimulation of neurotransmitter endorphin, resulting in positive feeling in the depressed person.[16]
- **Memory improvement:** positive effect on the brain is seen due to administration of hot chocolate, which helps in prevention of chronic or degenerative diseases like Alzheimer's disease.[17]

METHODOLOGY

CHOCOLATE MANUFACTURING PROCESSES

Chocolate manufacturing processes generally share common features such as:

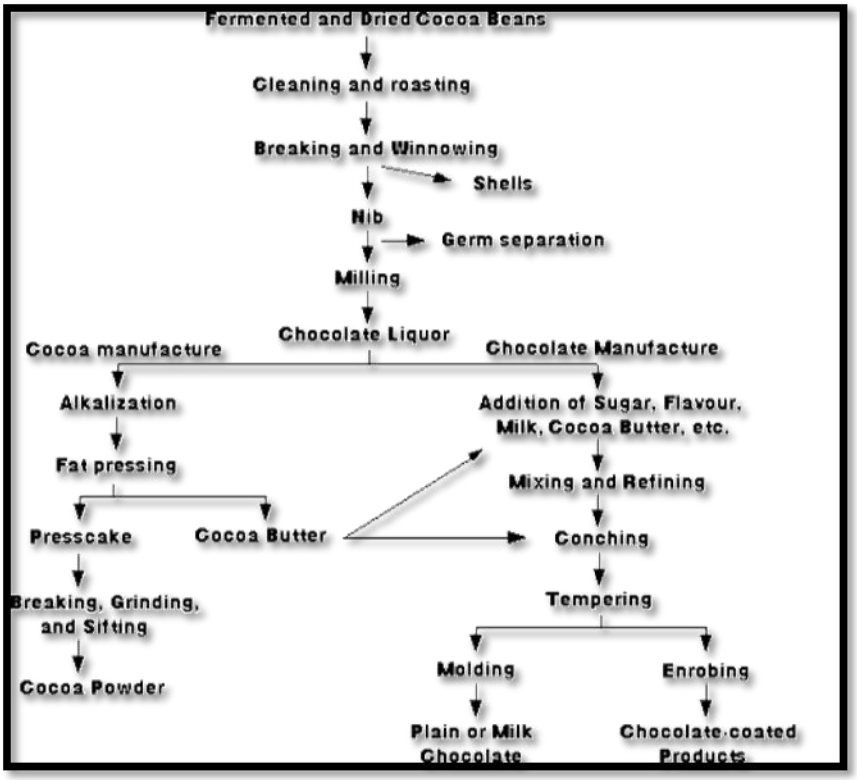
(1) Mixing

(2) Refining

(3) Conching of chocolate paste

(4) Tempering and depositing

(5) Moulding and demoulding.[18]



METHOD OF PREPARATION

Preparation of chocolate base

Oven is set to 50ºC. In a beaker, sugar and water is taken and kept in the oven for 4-5 min and syrup is prepared. Then cocoa butter is taken and kept in the beaker in the oven for 1 min. Then sugar syrup is removed from the oven, and cocoa powder is added and mixed well. Careful attention is paid to the chocolate manufacturing process to ensure that the temperature of the mixture is not too high. Then above mixture of chocolate base is cooled up to semisolid consistency and then flavor is added.[19-20]

Method preparation of chocolate

Oven was set at 50ºC, and then prepared chocolate base was melted until it becomes a free flowing liquid after required quantity of active pharmaceutical ingredient was added. Then it stirred continuously with the help of magnetic stirring for 10 minutes to ensure uniforms mixing. Then we poured the above mixture in a polycarbonate set mould and cooled for 15 minutes still it becomes solid.

Formulation of medicated chocolate

Prepared chocolate squares containing drug in appropriate quantity is known as medicated chocolate.[21-22]

EVALUATION PARAMETERS

EVALUATION OF CHOCOLATE BASE

1. Viscosity determination of chocolate base

Brookfield Rotational digital viscometer is used to measure the viscosity (cps) of the prepared chocolate base. The spindle is rotated at 20rpm; samples of chocolate base are heated at 50°C before the measurements are taken.

2. Taste, texture and mouth feel characteristics assessment

Taste, texture & mouth feel characteristics of chocolate are evaluated by taking panel of 10 human volunteers on a rating scale of 1-5.[23]

Characters	Criteria	Scale
Appearance	Glossy, even shine; no streaks, dots, cracks or "fog"	1-5 with 5 being the best.
Aroma or Smell	Chocolaty with only a light scent of any flavorings; fresh with no burnt, smoky, chemical smells	1-5 with 5 being the best.
Snap	Break clean without crumbling or layering; ideally a crisp pop when broken (loudest for dark chocolate)	1-5 with 5 being the best.
Taste	Chocolaty, flavors not overpower the chocolate taste. Good after taste	1-5 with 5 being the best.
Texture	Creamy and smooth, not waxy; promptly and evenly melts in mouth	1-5 with 5 being the best.

EVALUATION OF MEDICATED CHOCOLATE

General Appearance The general appearance of a chocolate formulation, its visual identity and overall "elegance," is essential (i) For Consumer acceptance (ii) For control of lot to lot uniformity and (iii) For monitoring trouble free manufacturing. The control of the general appearance of a chocolate involve the measurement of number of attributes such as chocolate's color, presence or absence of an odor, taste, surface texture and physical flaws.[24]

1. Dimension

The dimension of chocolate was measured by vernier's caliper.[25]

2. Moisture content determination

The moisture content of the chocolate formulation is determined by using digital Karl Fischer titration method. These instruments are designed to calculate the percentage (%) water content by using the formula,

$$water = \frac{\text{volume (ml)TS of water determination consumed} \times \text{f}\left(\frac{\text{mg}}{\text{m}}\right)}{\text{weight of sample(mg)}} \times 100\%$$

Where,

F= The number of mg of water (H2O) corresponding to 1ml of water determination TS,

TS= Water determination test sample.

3. Blooming test

a) Fat bloom

When the thin layer of fat crystal forms on the surface formulation. This will cause the chocolate to lose its gloss and soft white layer will appear, giving the finished article an unappetizing look. Fat bloom is caused by the recrystallization of the fat or a migration of filling fat to the chocolate layer. Storage at a constant temperature will delay the appearance of fat bloom.

b) Sugar bloom

This is a rough and irregular layer on top of the chocolate formulation. Sugar bloom is produced by condensation (when the chocolate is taken out of the refrigerator). This moisture will disintegrate the sugar in the chocolate. When the water evaporates afterwards, the sugar recrystallizes into rough, irregular crystal on the surface. This gives the chocolate an obnoxious look.

4. Drug-excipients interaction study

It is done by Differential scanning calorimetry.

5. Friability

Roche friabilator is used to measure the friability of the medicated formulation. It is expressed in percentage (%).

6. Melting point

It is calculated using a thermometer. On a tripod stand, a glass beaker half-filled with water was placed. To heat the water in the beaker, the burner was placed beneath the tripod stand. A porcelain disc containing medicated chocolate was placed on top of the beaker and melted by steam. A thermometer was attached to the porcelain disc.

7. Disintegration test

Disintegration time was tested in 900 ml of artificial saliva (pH 5.8) without disc at a temperature of 370°C and 50°C. These six individual chocolates were chosen at random and timed, then average weights were determined and the time in seconds for total disintegration of the formulation was recorded.[26]

8. In vitro drug release

It's done in a type 1 USP dissolution device (Basket). At 37±5°C and 50 rpm, dissolution tester bowels were filled with 900 ml of 0.1N HCl dissolution medium. The formulation was placed in the basket at intervals of 1, 2, 3, and up to 10 minutes, after which a 10 ml sample was extracted and replaced with an equivalent volume of fresh medium. UV Spectroscopy is used to analyze the gathered materials several sample are withdrawn from basket and volume is replaced with an equivalent quantity of fresh medium. The collected samples are filtered and analyzed by UV spectroscopy.

9. Stability test

It is the responsibility of the manufacturers to see that the medicine reaches the consumer in an active form so that stability of pharmaceutical is an important criterion. Stability of medicinal product may be defined as the capability of the particular formulation in a specific container to remain within its physical, chemical, microbial, therapeutic and toxicological specification, i.e. Stability of drug is stability to resist detoriation .90% of labeled potency is generally recognized as the minimum acceptable potency level. Detoriation of drug may take several forms arising from changes in physical, chemical and microbiological properties. The changes may influence the therapeutic value of preparation or increase its toxicity.

10. Accelerated stability testing

Since the period of stability testing can be use long as two years, it is time consuming and expensive. Therefore it is essential to devise a method that will help rapid predication of long-term stability of drug. The accelerated stability testing is defined as the validated

method by which the product stability may be predicated by strong of the product under condition that accelerated the changes in defined and predictable manner. The stability studies of formulated formulations were carried out at 25/75(℃/RH) and 2-8℃ for one month. The effect of temperature, humidity and time on the general appearance of chocolate and drug content were evaluated for assessing the stability of the prepared formulations.[27]

CONCLUSION

Foods that improve health or function are the newest craze in the food manufacturing industry. These foods prevent illnesses such as heart disease, osteoporosis, cancer, diabetes, etc. Epidemiological studies have shown that consumption of diets rich in fruits promotes lower risk of chronic diseases, including cancer, heart disease, stroke, and also diabetes control and reduced risk of obesity. Chocolate flavor is found in non-volatile substances that affect taste perception in addition to a volatile aromatic fraction of flavor-active ingredients. The genotype of the cocoa bean, in particular the amounts of polysaccharides, polyphenols, and storage proteins, determines its complex composition. Chocolate can mask the bitter and unpleasant flavors of drugs' organoleptic characteristics. Therefore chocolate drug delivery is a promising tool for delivery of drug through oral route.

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