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REVIEW ON MEDICATED CHOCOLATE TAKES A PATIENT-CENTERED APPROACH TO DRUG DELIVERY

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ABSTRACT
The goal is to create medicinally beneficial chocolate that has no negative side effects. Cocoa, a basic ingredient in many chocolate formulations, was substituted for carob (Ceratonia siliqua) since it requires a large amount of sugar in the formulation and includes caffeine, which stimulates the CNS. Carob is high in natural sweeteners, has no fat, caffeine, or oxalates, and is high in antioxidants, which assist to prevent a variety of ailments. Many traditional drug delivery systems are ineffective for paediatric patients because their developmental state and dosing requirements differ from those of other groups of people. Age-appropriate medicines require technological platforms to ensure patient acceptability while maintaining safety, efficacy, accessibility, and affordability. Recent methods and accomplishments in the field of age-appropriate drug delivery for paediatric patients are discussed, including patient-centric formulations, administration devices, and packaging solutions

INTRODUCTION

Chocolate is an anhydrous media resistant to microbial growth and hydrolysis of water-sensitive active agents because it contains saturated fat, polyphenols, sterols, di and triterpenes, aliphatic alcohols, and methylxanthines. Infants and children have a sweet-taste preference that declines in late adolescence compared to adults. Bitter flavour is likely to impair acceptance if a dislike for bitterness develops at a young age. To circumvent these restrictions of bitter taste, researchers have devised a novel solid dosage form of drug delivery system, such as medicated chocolate and medicated lozenges, to prevent hazardous intakes in young children. Medicated chocolate has a more appealing texture and enhances patient consent, making it more appealing to children. Geriatrics and people with dysphagia benefit from this type of delivery technology [1]. Chocolate is a versatile food that may be combined with drugs to generate entirely new flavour and tactile experiences. Phenyl ethylamine is a chemical that occurs naturally in the brain and is known as "love drug" because it causes feelings of happiness and contentment. Sweet taste is used to detect extremely calorific saccharides that can be consumed. A chocolate basis is used to make medicated chocolate, and the medicine is mixed into the chocolate base. Chocolate medication delivery system refers to a drug that is incorporated into chocolate and then released from the chocolate [2].

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Nutrition in cocoa, carob in chocolate:

Vitamins E, D, C, Niacin, B6, and folic acid are abundant in carob powder; vitamins A, B2, and B12 are present in smaller amounts. Oleic, linoleic, palmitic, and stearic acid are among the 17 fatty acids found in carob powder oil. Carbohydrate, Water, Protein, Lipid, Cholesterol, Sugar, Total Fibers, Sodium, Potassium, Iron, Calcium, Phosphorus, Thiamine, Vitamin A, Theobromine, Phenolics, and Energy are all found in cocoa powder [4].

Evaluation

1. ***Visual identity and overall elegance:*** It's necessary for preserving batch-to-batch consistency, ensuring trouble-free manufacturing, and gaining eater acceptability. The general appearance entails Dark Brown in colour. odour - chocolate without the bitterness, no smokiness, Taste - Slightly sweet, but not overly so. Smooth and even surface texture Vernier's callipers are used to measure diameter and height [3].
2. ***Hardness or crushing strength:*** Monsanto Hardness Tester or Pfizer Hardness Tester are used to determine how much force is required to break the tablet. Kg/cm2 is the unit of measurement. To accomplish so, we must randomly select a number of medicated chocolates from each batch, determine their hardness, and calculate the mean [5].
3. ***Viscosity determination:*** Before taking measurements, the spindle of a Brookfield rotating viscometer was revolved at 50 rpm and the chocolate base was heated to 50°C [1].
4. ***Drug-excipients interaction study:*** It is done by Differential Scanning Calorimetery (DSC) [3].
5. ***Drug content determination:*** The UV Spectrometer is used to determine it. In a beaker, medicated chocolate is combined with a dissolving solvent. This liquid is sonicated for good mixing in a bath sonicator, and then placed into a centrifuge tube for 15 minutes at 2500rpm. Centrifugation separates two layers, one of which is clear liquid and the other of which is a solid chocolate basis. This supernatant is next filtered to remove any leftover traces of chocolate. The liquid sample is then compared to the dissolving solvent as a blank using a UV spectrophotometer. Thin Layer Chromatography is another method of determining it. TLC plates were made using silica G and then activated for 12 hours. Using capillary, spotting was performed on both the control and test plates. Both plates should be run in the same mobile phase, which is a 7:3:2 mixture of toluene, ethyl acetate, and water. After running both plates, the plates are air dried. The iodine chamber was used to visualise both plates. Drug content is measured by comparing the RF values of both plates [6].

   Sugar Bloom: It occurs when chocolate comes into touch with moisture, causing the sugar on the chocolate's surface to dissolve. Condensation develops a rough and uneven layer on top of the chocolate composition when it is removed from the refrigerator. When water evaporates from sugar, it recrystallizes into rough, uneven crystals on the surface, giving it an unappealing appearance. The test sample was given 30^0 c for 11 hours, then 180^0 c for 11 hours. After that, the test sample was examined. When the water evaporates, the dissolved sugar crystallises and settles on the chocolate's surface. The dusty appearance of the chocolate coating is due to these microscopic sugar crystals. Sugar bloom can be avoided by storing at a consistent temperature [7].
6. ***Physical stability to ensure physical stability, a sample of*** chocolate was maintained in a sealed container at 280°C for one month. After a month, a test sample of chocolate was tested for physical appearance and drug degradation. [5].
7. ***Moisture content determination:*** It is determined by using Digital Karl Fischer Titrator model. These instruments are designed to calculate percentage (%) water content by using formula: Water = [Volume of water determination test sample x number of mg of water corresponding to 1mL of water Determination TS (mg)] x 100 (%).

   Another way moisture content is determined by using a Desiccator. The medicated chocolate weighed and kept in a desiccator containing anhydrous silica gel. After 24 hrs, formulations were taken out, weighed and % moisture loss was calculated by [6]

$$\%\ Moisture\ los = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

8. ***Viscosity determination of chocolate base:*** it is measured by using a rotational digital viscometer. The spindle was revolved at 20 revolutions per minute, and chocolate base samples were heated to 50^0 c before the measurements were collected [4].
9. ***Drug-excipients interaction study:*** It is done by Differential scanning calorimetry [4]
10. ***Physical observation:*** It's carried out to see whether any interactions or physical changes occur when different

excipients are maintained in different conditions. Drug is combined in a 1:5 ratio with various excipients and stored in closed vials. For one month, these vials were kept at 25°C. The vials were stored at a temperature of 2-8°C. Each test group's sample vials are withdrawn after one month and analysed for physical appearance and drug degradation [7]

11. ***Stability test:*** It's the ability of a formulation in a certain container to keep within its physical, chemical, microbiological, medicinal, and toxicological standards. The lowest allowable potency level is 90 percent of the labelled potency. The alterations may have an impact on the preparation's medicinal value or raise its toxicity. Aluminium foil, wax paper, and a double wrapper are used to package the product. For one month, stability tests were conducted at ambient temperature (25–20°C) and in the refrigerator (20–80°C). The samples were then analysed in preparation for the evaluation test [5] [6]
12. ***Accelerated stability testing:*** Because stability testing can take up to two years and is costly, it is necessary to forecast the drug's long-term stability quickly. It's characterised as a situation in which product stability may be predicted by storing the product under settings that accelerate change in a specified and predictable way [4]
13. ***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 analyse the gathered materials [7]
14. ***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 [5] [6].
15. ***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 [6]
16. ***Friability:*** Roche friabilator is used to measure the friability of the medicated formulation. It is expressed in percentage (%) [7]

Significance of Medicated Chocolates

Bypassing the liver's first-pass metabolism and the GIT's pre-systemic elimination. Water-sensitive medicines are resistant to microbial development and are degraded by hydrolysis. Improve patient consent, which is well received by kids. Absorption of drugs is quick. Shows both a local and a systemic impact. Simple to prepare [8]

Benefits of Chocolate

Flavanol-rich chocolate can aid to prevent cardiometabolic illnesses, improve cardiovascular outcomes, and reduce insulin resistance, all of which contribute to glucose homeostasis by slowing carbohydrate breakdown and absorption in the stomach. Dark chocolate helps to prevent WBCs from attaching to blood vessel walls and reduces the risk of tooth decay and atherosclerosis. It also increases blood flow to the brain and heart, and includes phenylethylamine (PEA), which stimulates the brain to produce endorphins. It also contains the mild stimulant caffeine, which is used to treat mood problems. Theobromine, a mild stimulant found in chocolate, aids in cough relief by suppressing vagus nerve activity.

Dark chocolate contains antioxidants that help to prevent plasma lipid oxidation, as well as flavonoids and polyphenols that help to control uncontrolled cell division and reduce inflammation by neutralising free radicals [9]. Dark chocolate keeps blood vessels healthy, and good circulation keeps type 2 diabetes at bay [10] [11]. Cocoa extracts and procyanidins inhibit pancreatic -amylase, pancreatic lipase, and secreted phospholipase A2 in a dose-dependent manner [12]. By boosting glucose transport and insulin signalling proteins in insulin-sensitive tissues (liver, adipose tissue, and skeletal muscle), cocoa and its flavanols prevent oxidative and inflammatory damage (liver, adipose tissue, and skeletal muscle) [13]. Some studies have found that cocoa has anti-obesity and anti-metabolic syndrome properties, such as smelling dark chocolate eliciting a positive response and lowering appetite, preventing weight gain [14] [15]. Flavonoids promote metabolic events that reduce lipogenesis, lipolysis initiation, adiponectin secretion, lowering lipid deposition and insulin resistance [16] [17]. A meta-analysis revealed that cocoa chocolate has no effect on weight, BMI, or waist circumference

[18]. Dark chocolate may have beneficial effects on lipid profiles when combined with nutraceuticals [19]. According to a study almonds, dark chocolate, and cocoa in one's diet without exceeding daily energy requirements can lower the risk of coronary heart disease [20]. Dark chocolate/cocoa can lower LDL cholesterol levels in a meta-analysis for a short period of time (2–12 weeks), but has no effect on high-density lipoprotein HDL or triglycerides [21]. In a placebo-controlled cross-over research, daily consumption of cocoa flavanol-containing chocolate bars with added plant sterols reduced total LDL cholesterol levels in the blood [22]. Due to its beneficial effects on HDL cholesterol and inflammation indicators, dark chocolate consumption raises HDL cholesterol levels, lowers LDL/HDL cholesterol ratio, and controls atherogenic profile [23].

Intestinal microbiota harvests in the human gut, a huge collection of microbes with a key role in energy storage and metabolic disorders [24]. In the small intestine, flavanol monomers and dimers are absorbed, and procyanidins are destroyed by the colonic flora, resulting in the creation of phenolic acids, which are subsequently absorbed, digested, and eliminated in the urine or faeces [25] [26] [27]. Epicatechins, catechins, and procyanidins are found in cocoa. A high intake of dietary flavonoids, a subgroup of polyphenols, may reduce the risk of coronary heart disease. [28]. Consumption of cocoa on a regular basis helps to alleviate health problems caused by allergic reactions. Multiple allergic processes have been connected to the positive effects of cocoa flavonoids on the immune system, including decreased mediator release, restored T-helper 1 and T-helper 2 cell balance, and decreased IgE production [29]. Vasodilation and increased cerebral blood flow provide oxygen and glucose to neurons, causing the hippocampus to grow additional blood vessels [30] [31].

The antioxidant activity of polyphenols may aid in the treatment of various neurological diseases [32] [33]. The social and psychological backdrop of daily living has an impact on metabolic health, emotions, and moods, and it can influence dietary choices [34]. Chocolate consumption can help to alleviate depression in the form of hysteroid dysphoria, which is characterised by repeated episodes of depression as a result of feelings of inadequacy or rejection in social situations. Drug-responsive symptoms increase serotonin transmission through central serotonin pathways [35][36][37][38]. Carob powder, a key component of chocolate, has antibacterial and antifungal properties. It also has anti-diarrheal, anti-emetic, and anti-diarrheal properties. It has a lot of antioxidants. Carob powder possesses neuroprotective, cardioprotective, & hepatoprotective properties. It has the ability to cure metabolic syndrome and has skin protection properties. It also aids fertility (male) [39] [40]. Resistance sugar is a type of dietary fibre that is also utilised in chocolate formulation. It promotes probiotic flora, has hypoglycaemic and hypocholesterolemic effects, aids in energy and weight management, and aids in mineral absorption [41] [42]

STEPS TO PREPARE MEDICATED CHOCOLATE

Preparation of chocolate base

1. Ingredient for chocolate base was weighed and sieved (sieve no: 30).
2. Place the beaker containing sugar /resistance sugar and water to prepare the simple syrup for 4 to 5 min.
3. Melt the cocoa butter and lecithin in a beaker and add the simple syrup and then this mixture added to cocoa powder / carob powder and mix well until it becomes free-flowing.
4. After cooling add the flavouring agent and it is poured into a polycarbonate set mould. Then allow to solidify in a refrigerator [42].

Preparation of Medicated chocolate

1. The oven is preheated at 50°C to melt the chocolate base.
2. Then required quantity of drug have to add to chocolate base and mix well by using a magnetic stirrer.
3. Then add required quantity of the preservatives.
4. Then pour the above mixture into mould and put it in a refrigerator [43].

CONCLUSION

Due to the complexity of creating chocolate compositions that contain particle active agents, chocolate formulation has not received commercial acceptability for delivery of pharmaceutical or nutraceutical agents. Chocolate dosage forms, on the other hand, have been discovered to be formulated by carefully regulating the particle size of the particulate active ingredient. Chocolate's organoleptic properties are ideal for disguising disagreeable flavours associated with some active agents and providing a smooth and creamy texture to active agent compositions. As a result, chocolate formulations provide an appealing way to give medications orally.

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Nil

CONFLICT OF INTEREST
The authors declare no conflict of interest.

AUTHOR CONTRIBUTION
Moumita Paul, Priyanka Ranabhat and Deepika Khatiwara designed the work and made necessary corrections and revisions in the manuscript. Arnab Bagchi collected the content and did literature review and also contributed in drafting the manuscript. All the authors framed the final manuscript

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