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A REVIEW: MEDICATED CHOCOLATE AS A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

This review explores the emerging trend of utilizing medicated chocolate as a novel drug delivery system. With a focus on medicated chocolate's potential applications and health benefits, the paper delves into the unique properties of chocolate that make it a promising carrier for various pharmaceutical compounds. The review focuses on the formulation techniques employed in developing medicated chocolate, addressing challenges such as taste masking and stability. Furthermore, the review highlights recent research findings on the effectiveness of medicated chocolate in delivering drugs, especially in pediatric patients. The potential advantages, including improved patient compliance and the ability to mask bitter tastes and odours, are discussed. Various tests and parameters for the evaluation of medicated chocolate is also involved in the review. The paper concludes with an overview of the currentstatus and future prospects of medicated chocolate as a viable and palatable drug delivery system.

KEYWORDS: Medicated Chocolate, Paediatrics, Taste Masking, Curative Chocolate, Novel Drug Delivery System.

1. INTRODUCTION

Drug delivery systems can be defined as a method to deliver drugs to humans or animals.[14] Oral drug delivery is considered one of the best routes of drug administration for patients. In addition, it also has certain advantages and disadvantages.[3] In the case of children, compliance with medication is one of the important factors. The repetitive administration of

drugs in children is considered to be one of the difficult tasks and sometimes may lead to medication non-adherence. To overcome this, medicated chocolate is thought to be one of the accepted forms of oral route of drug administration in children or paediatrics as it increases patient compliance due to the unique taste, texture, and palatability of chocolate.[1]

Given that many Active Pharmaceutical Ingredients (APIs) possess a bitter, unpleasant, and disagreeable taste, creating palatable dosage forms becomes crucial through taste-masking approaches. Consequently, medicated chocolate emerges as a preferable option for paediatric patients, enhancing acceptability. Furthermore, extensive research has identified and studied the significant health benefits associated with chocolates.[16]

Medicated chocolate is characterized as a dosage form wherein drugs are incorporated into the chocolate base in appropriate quantities. Chocolate, known for its sophistication and adaptability, can be crafted into diverse consistencies and flavours.[13] Chocolate is typically crafted from cocoa butter, cocoa beans, the dried and fermented seeds of *Theobroma cocoa*.[8] It commonly possesses a brown hue, with sweeteners added to mitigate its inherent bitterness, often flavoured with vanilla.[9] Chocolates are categorized as dark, milk, or white, depending on the proportion of cocoa utilized in their formulation.[2]

Chocolate serves as a water-resistant medium for active agents that are sensitive to moisture, exhibiting resistance to both microbial growth and hydrolysis. In numerous aspects, chocolate proves to be an outstanding carrier for delivering these active agents.[1] Chocolates typically contain cocoa powder derived from cocoa beans, is also considered to have anticariogenic agents.[15] Tooth decay, caused primarily by a microorganism called *Streptococcus mutans*, involves the production of the glucosyltransferase enzyme (GTFB, GTFC, and GTFD), which adheres to teeth and leads to decay. The cocoa bean and its husk are rich in theobromine, a major component with two significant characteristics: anti-glucosyltransferase activity and anti-microbial activity.[15] This anti-glucosyltransferase activity offers protection against tooth decay, contributing to an anti-cariogenic effect. An innovative strategy involves the development and production of heat-resistant chocolate, specifically designed for the extended use of medicated chocolate in summer seasons and tropical climates.[18] This can be achieved by extending the melting point of medicated chocolates to maintain a solid consistency in elevated temperatures.[18]

1.1. Physical properties of chocolate

Cocoa butter typically possesses a melting point ranging from 34-38°C.[9] Consequently, chocolate maintains its solid form at 25°C but melts upon contact with the warmth of the mouth. Refrigeration is essential to preserve this temperature stability. Overheating cocoa butter should be avoided, as it can result in the formation of less stable chocolate due to polymorphism.[9] The refractive index of cocoa butter is 1.44, with an acid value of 1.68 and a saponification value of 191.214.[9] Natural cocoa powder has a pH ranging between 3.5 to 5.8 and processed cocoa powder has a pH range between 6.8 to 8.1.[8]

1.2. Chemistry of Chocolate

Comprising cocoa, chocolate encompasses around 300 volatile compounds, encompassing aliphatic esters, polyphenols, aromatic carbonyls, and theobromine. The pharmacologically active elements within cocoa seeds include amines, alkaloids, fatty acids, polyphenols (specifically flavonoids), tyramine, trigonelline, magnesium, phenylethylamine, and N-acylethanolamines.[2]

1.2.1. Alkaloids - In its raw state, the cocoa bean contains approximately 2-3% theobromine, a principal alkaloid, along with methylxanthines (4%), caffeine (0.2%), and traces of theophylline. These alkaloids predominantly contribute to the bitter taste associated with cocoa.[19]

1.2.2. Polyphenols -Approximately 15% of polyphenols are found in cocoa seeds, contributing to the astringent sensation and fruity flavour of chocolate. The three primary polyphenols present are catechins (29-38%), anthocyanins, and proanthocyanidins (58-65%).[19] Other minor polyphenols include flavones and polyphenolic acid.[19] These polyphenols play a role in the beneficial effects of cocoa on cardiovascular disorders.[9]

1.2.3. Proteins - Cocoa comprises around 10-16% protein.[19]

1.2.4. Carbohydrates -Cocoa beans contain about 2-4% free sugars such as glucose, fructose, sucrose, galactose, mannitol, inositol, and arabinose, and approximately 12% of polysaccharides such as starch, pectin, cellulose, and mucilage.[19]

1.2.5. Minerals -Minerals such as potassium, phosphorus, copper, zinc, iron, magnesium havebeen found in cocoa.[2]

1.2.6. Other components -Volatile components present are cocoa include alcohol, aldehydesand ketones, esters, pyrazines, acid, and phenols.[19]

1.3. Types of chocolate[2,13]

The various types of chocolate used in the chocolate preparation are as follows:

1.3.1. Sweet chocolate – It should contain not less than 30% total cocoa solids out of which 18% should be cocoa butter and 12% cocoa solids.[13]

1.3.2. Milk chocolate – it should contain not less than 25% cocoa solid and a minimum quantity od 12-14% of milk solids.[13] Typically, a blend of medium-roasted West African beans and Ecuadorian beans is commonly used.[2]

1.3.3. Couverture chocolate – it should contain not less than 35% of cocoa solids out of whichnot less than 31% of cocoa butter.[13]

1.3.4. Milk chocolate couverture – it should contain not less than 25% cocoa solids, not lessthan 14% milk, and not less than 31% total fat.[13]

1.3.5. White chocolate – it should contain not less than 20% cocoa butter and not less than 14% milk solid.[13]

1.3.6. Bittersweet chocolate – This type is employed for creating highly flavoured, sweet cream centres with a bitter coating.[2]

1.4. Health benefits of chocolate

In dark chocolates, due to the presence of varying percentage of polyphenols there is an increase in the nutritional and pharmacological aspects of the chocolate.[20] The various health benefits of chocolate have been listed below.

1.4.1. Cardiovascular diseases -Foods abundant in flavanols are recognized for their potent cardioprotective effects, reducing the risk of diverse cardiovascular diseases. Consequently, the presence of flavan-3-ols in cocoa suggests its potential utility in managing cardiovascular diseases to a certain extent.[9] Dark chocolate, in particular, proves beneficial for preventing and controlling atherosclerosis by contributing to the thickening and hardening of arteries while restoring their flexibility.[9] Cocoa products exhibit properties that can help prevent cardio-metabolic disorders, assumed to impose a burden on the patient's heart.[8]

1.4.2. Hypoglycaemic action -For individuals with diabetes, dark chocolate supports the maintenance of healthy blood vessels and offers protection against type 2 diabetes mellitus. The presence of flavonoids in dark chocolate can enhance insulin resistance in diabetic patients. Additionally, the low glycaemic index of dark chocolate reduces the risk of sudden spikes in sugar levels.[8]

1.4.3. Magnesium deficiency -Cocoa is considered among the food's rich in magnesium, widely consumed by a large population globally. An experiment conducted on rats suggested that cocoa products could be utilized in treating chronic magnesium deficiency in rats.[4] However, the impact of cocoa on humans is yet to be thoroughly investigated.[8]

1.4.4. Diuretic action -The theobromine found in cocoa functions as a diuretic, aiding in the treatment of oedema by facilitating the removal of excess water and salts from the body. This property is beneficial in the management of hypertension.[17]

1.4.5. Anticancer action -Dark chocolate is thought to offer potential relief from cancer, with ongoing studies aimed at identifying the specific pharmacological agent responsible for this effect.[1]

1.4.6. Antioxidant action -Dark chocolate is acknowledged as a substantial source of antioxidants, safeguarding cells from oxidative damage.[2] The existence of free radicals can accelerate the aging process and pose a potential risk of cancer, but dark chocolate may aid in their prevention.[2]

1.4.7. Vitamins and minerals -Dark chocolate is abundant in vitamins and minerals, including the B-vitamin complex (B1, B2, B3, B9), vitamin K, and minerals like calcium, magnesium, manganese, phosphorus, iron, copper, potassium, zinc, and selenium. The presence of copper and potassium contributes to the protection against cardiovascular disorders.[2]

1.4.8. CNS action -Dark chocolate enhances blood flow to the brain, making it potentially beneficial in the treatment of various central nervous system disorders, including mood swings. Dark chocolate contains Phenylethylamine, which stimulates the release of endorphins, thereby improving the patient's mood.[8]

1.4.9. In oral hygiene -The presence of theobromine in dark chocolate offers protection againstdental cavities by strengthening tooth enamel, thus contributing to maintaining proper oral hygiene.[9]

1.4.10. Neuroprotective action -Experimental data from numerous researchers suggests that dark chocolate, abundant in polyphenols, possesses neuroprotective, neuromodulatory, and neurorescue activities, effectively preventing neurodegenerative disorders.[19]

2. Method of preparation of medicated chocolate

2.1. Formulation of chocolate base

Initially, preheat the hot air oven to 50°C and maintain this temperature for the required duration.[3] Weigh and sieve the ingredients for the chocolate base using a No. 30 sieve.[5] Combine sugar and water in a beaker, creating a simple sugar syrup by placing it in the oven for 4-5 minutes.[17] Melt cocoa butter in a beaker by placing it in the oven for 1 minute.[17] Add the prepared simple syrup to the beaker containing cocoa butter, along with the required quantity of cocoa powder, and mix thoroughly. Careful mixing is essential to ensure the chocolate manufacturing process occurs at an optimal temperature.[3] Allow the mixture to cool to a semisolid consistency before adding the flavouring agent.[5] Pour the mixture into mould and refrigerate for solidification.[5]

2.2. Formulation of medicated chocolate[5]

The oven is preheated at 50°C. Melt the required amount of chocolate base by placing it in the oven. The required quantity of the drug is incorporated to the base and then mix thoroughly by stirring or by use of a magnetic stirrer. Then add the required quantity of preservatives if any. Then lastly after cooling, pour the semisolid consistency of medicated chocolate into the moulds and refrigerate it to solidify.

3. Evaluation tests

3.1. Evaluation test for chocolate base

3.1.1. Viscosity determination -Initially, the prepared chocolate base is melted at 50°C, and its viscosity is evaluated using a Brookfield viscometer.[10]

3.1.2. Taste, texture and mouth feel characteristics of chocolate base -The taste, texture, and mouthfeel characteristics of the chocolate base are evaluated by 10 human volunteers, and these attributes are subsequently rated on a scale of 1-5.[3]

3.2. Evaluation test for medicated chocolate

3.2.1. General appearance -This involves visually evaluating the colour, odour, taste, texture, and any potential flaws in the medicated chocolate.[11] Typically, the general appearance of chocolate includes a dark brown colour, a chocolaty aroma without a smoky taste, a slightly sweet flavour without bitterness or excessive sweetness, and a smooth and uniform texture.[5]

3.2.2. Dimensions and thickness -Vernier's calliper is used for the determination of dimensions and thickness of the medicated chocolate.

3.2.3. Blooming test

3.2.3.1. Fat bloom -The development of a thin layer of fat crystals on the surface of the medicated chocolate formulation is referred to as fat bloom.[17] This phenomenon results in the loss of gloss and the occurrence of a soft white layer, ultimately reducing the palatability of the medicated chocolate and giving it an unappetizing appearance.[13] The recrystallization of fats and the migration of fat to the chocolate layer are the underlying causes of fat bloom. Adequate storage at a consistent temperature can help in slowing down the appearance of fat bloom.[13]

3.2.3.2. Sugar bloom -Sugar bloom refers to the uneven and irregular layer that forms on the surface of a chocolate formulation. The primary cause of sugar bloom is condensation, often triggered when the chocolate is removed from the refrigerator. This moisture condenses and dissolves the sugar in the medicated chocolate. Upon evaporation, the sugar recrystallizes intorough and irregular crystals on the surface, resulting in an unappealing appearance.[13][17]

3.2.4. Melting point -Melting point of the medicated chocolate was determined by placing a 1x1 cubic cm chocolate in the melting point apparatus and the temperature at which it melts is determined.[6]

3.2.5. Drug content determination -UV spectrophotometer is used for the determination of frug content present in medicated chocolate.[10] It is determined at 260nm against blank.[11]

3.2.6. Drug excipient compatibility studies -Drug excipient compatibility studies are carried out using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared (FTIR). Itis carried out for both pure drugs used as well as for the medicated chocolate.[3][11]

3.2.7. Weight variation -According to USP, weight variation is evaluated by randomly selecting 5 formulations from each batch and then weighed individually. Then the average weight and the standard deviation is calculated and determined.[3]

3.2.8. Moisture content determination -Silica gel desiccators are employed to evaluate the moisture content of medicated chocolate. The process involves placing the medicated chocolate inside the silica gel desiccator, and after a 24-hour period, the medicated chocolate is weighed. Subsequently, the percentage of moisture content is calculated using the formula.[1]

Percentage moisture loss (%) = initial weight – final weight / initial weight x 100[1]

3.2.9. Disintegration test -In accordance with the USP standards, the disintegration test for medicated chocolate is conducted utilizing a disintegration tester apparatus at a temperature of 37±0.5°C, with a speed of 60 rpm, and using a buffer of pH 6.8 for a duration of 20 minutes.[11]

3.2.10. In vitro drug release studies -The dissolution test for medicated chocolate is conducted using a USP type II dissolution tester apparatus.[11] The procedure is carried out at a temperature of 37±0.5°C with a speed of 50 rpm. Initially, the baskets of the dissolution tester apparatus are filled with 900 ml of 0.1N HCl. Subsequently, the formulation is placed in the basket at intervals of 5, 10, 15, 20, up to 60 minutes. The samples are then replaced with an equal amount of fresh medium. Following this, the samples are evaluated and analysed using a UV spectrophotometer at 260nm.[5][11]

4. CONCLUSION

From the information presented above, it suggests that medicated chocolate holds considerable potential as an innovative method for drug delivery in children. Medicated chocolate, with its numerous health benefits, emerges as an optimal choice for improving patient compliance. Moreover, it provides advantages in concealing the bitter taste and disagreeable odour of drugs, offering a pleasingly smooth texture and consistency. As the pharmaceutical industry seeks alternatives to conventional drug delivery methods, medicated chocolate is poised to play a significant role, offering a convenient, pleasant, and potentially more effective means of administering medications. The evolving research and positive outcomes in this field forecast a bright future for medicated chocolate, making it a focal point of interest in the continued exploration of innovative drug delivery solutions.

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5. Author's contribution

The authors have equally contributed to the preparation of the review article.

6. Conflict of interests

The authors have declared no conflicts of interest pertaining to the publication of the review article.

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