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A REVIEW ON MEDICATED CHOCOLATE FOR PEDIATRICS

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ABSTRACT

For years, chocolate/cocoa has been prized for its flavor and potential health benefits. Because most medications are bitter, oral delivery of these medications results in patient noncompliance, particularly in children. To solve these limitations, it is proposed that a dosage form be developed that is most suitable for pediatric patients. We designed a chocolate medicine delivery system since chocolate is one of the most palatable and favorites foods for kids. A chocolate base is used to make medicated chocolate, and the medicine is then added to the base. The appearance, moisture content, viscosity, blooming test, drug content determination, and in vitro drug release of the medicated chocolate can all be investigated. This review focused on the health benefits and applications of both medicated and non-medicated chocolates.

KEYWORDS: Medicated chocolate, Oral Drug Delivery System, Pediatrics chocolate.

INTRODUCTION

Every prescription nowadays contains several divisions of pharmaceuticals that must be delivered at regular intervals, most commonly by oral route. This type of repetitive oral administration of multiple treatments makes the patient uncomfortable due to swallowing difficulties. This is particularly true when it comes to children Therefore, most pharma companies are coming out with several modification formulations such as dissolving tablets, dry syrups, lozenges, oral films and so on, with the goal of allowing patients of any age to administer many medicines with easily, hence enhancing patient compliance. Apart from the dose form, the drug's organoleptic qualities must be considered carefully during the manufacturing process. Patient compliance can be increased by delivering active pharmacological ingredients in a visually attractive manner, which reduces rejection and

psychological inhibition toward dosage forms. With all that in perspective, a new interesting and widely accepted form of formulation has been produced. Contrary to popular perception, chocolate is not just for kids even older men and women can't seem to resist this mouthwatering taste.[1]

Oral Drug Delivery System for Pediatrics

For pediatrics, the oral drug administration route can be extremely difficult due to their continuous growth. The new medicine delivery approach is intended to overcome issues related to physiological impairment and swallowing difficulties. For a broad range of medicines and clinical aspects such as quality, safety, and efficacy of designed formulations, the evolution of an oral drug delivery system is exceptionally hard. The demands, needs, and good qualities of pediatrics formulation make it difficult to develop. Just because the pharmacokinetic and pharmacodynamic properties of oral drugs change as children grow, dose flexibility is required for the success of all age groups of children. Patients will find oral preparations to be reasonable and efficient.[2]

The diversity of children, taste masking, stability – physical, chemical, and microbiological, reaching global regulatory acceptability, delivering immediate patient access, and faster development timelines are important barriers for designing pediatric formulations. The optimization of oral drug administration has been one of the most difficult tasks in pediatric pharmacology. The speed or quantity of drug absorption, and thus bioavailability, may be affected by crushing tablets. The widely used method is cutting tablets, which may be suitable for some medications but can introduce significant variability between dosages. Extemporaneous oral suspension or solution may have issues with stability, handling, the insertion of a flavoring agent, or the use of a different brand, which all can affect the final product's stability or the drug's absorption characteristics. For infants and kids, commercially produced oral liquid drugs provide a more dependable, ready-to-use preparation, but bioequivalence with solid oral dose forms is still unknown. The issues with currently available formulations highlight the need for new products that are both simple to use and capable of providing consistent serum drug concentrations and a better taste.[3]

CHOCOLATE

It is a complex and adaptable food that may be combined to create a wide range of taste and consistency sensations. Chocolate is an anhydrous medium for water-sensitive active agents that is resistant to microbial growth and hydrolysis. In many ways, chocolate is an excellent

vehicle for delivering active agents. The organoleptic characteristics of chocolate, for example, are suitable for mask unpalatable flavors associated with some active agents and delivering a smooth and creamy texture to otherwise unappealingly abrasive active agent formulations**.**

Saturated fat, polyphones, sterols, Di and triterpenes, aliphatic alcohols, and methylxanthines are all prevalent in chocolate. Chocolate's main constituent is cocoa, which is high in polyphones, especially flavan-3-ols like epicatechins, catechins, and procyanidins. A high intake of dietary flavonoids, a subgroup of polyphenols, may reduce the risk of coronary heart disease, according to research.[4]

Antioxidants protect cells from free radical damage produced by biological functions like breathing and external impurities like cigarette smoke. Free radicals cause damage to our bodies when we don't eat enough antioxidants. Increased oxidation, for example, might cause plaque to form on the artery walls due to low-density lipoprotein (LDL), generally known as "bad" cholesterol.[5]

“The sense of flavor perceived in the tongue in contact with a substance” is how taste is defined. A palatable food or drug is one that has a nice flavor. There are four fundamental taste modalities: sweet, salty, sour, and bitter. The primary cells for taste are modified epithelial cells that are organized in taste buds and found in the taste papillae of the tongue. Childrens’ taste sensations differ from adults' infants, and children have a preference for sweet-tasting substances that decreases to resemble that of adults by late adolescence. Bitter aversion, on the other hand, develops from an early age and, as a response, bitter flavours are more likely to be unpleasant. Indeed, addition of aversive bettering agents has been proposed as a method of preventing toxic ingestions in young children.[6]

Chocolate contains lecithin, a well-known natural emulsifier used in chocolate production to give it its specific rheology. Lecithin is a well-known natural emulsifier that has been used in the manufacture of micro/ nano emulsions alone or in combination with surfactants to improve the aqueous solubility of several medications.[7]

Soya lecithin is a kind of phospholipids found in soya beans. It is essentially an industrial waste product that is recovered from the sludge that remains after the degumming of soya oil. This is why soya lecithin is the most popular type of lecithin on the market; it is a waste

product that can be simply and cheaply obtained from soya bean oil production. Mostly in liquid form, it shows as a yellow-brownish fatty fluid with a rather thick viscosity. Because of the polymorphic nature of cocoa butter, it is necessary to temper the chocolate melt during the manufacturing process in order to obtain the best crystal shape, known as Form. Emulsifiers are used to improve the rheological qualities of chocolate formulations. To reduce the plastic viscosity of the bulk, soya lecithin containing 62 to 70 percent phospholipids is added. Usually used at a concentration of 0.1 to 0.3 percent, lecithin has a minimal effect on yield stress. 0.3 to 0.5 percent of the population. While soya lecithin takes only a few minutes to incorporate, the best time to add it to the chocolate is near the end.[6]

Chocolate also has medical benefits, such as lowering blood pressure, changing blood flow to the brain, preventing cell damage, and improving glucose levels. It also reduces the risk of heart attack, improves HDL cholesterol, and lowering LDL cholesterol.[8]

However, chocolate has multiple benefits such as a rapid initiation of action, ease of manufacture and scale, reduced drug dose, and increased drug loading capacity.[9]

Types of Chocolates

- **Milk chocolate:** It is recommended that you use mostly medium roast West African beans with Ecuadorian beans. This blend would produce a clean, nutty, slightly fruity chocolate. It's important to remember that the addition of the more acidic Brazilian and Malaysian beans should battle with the desired creamy flavors.
- **Light milk chocolate:** This product could be prepared with slightly roasted java beans, which have a light color and a mild overall flavors with strong nutty overtones.
- Because the coating is many shades lighter than a 100 % pure West African bean, this would aid in obtaining a good standard of identity for milk chocolate.[10]
- **High-quality semisweet chocolate:** To highlight ideal notes and reduce burnt/bitter notes, use mostly West African stock (light to medium roast) for its chocolate flavour and slightly nutty undertones. When mixed with Caracas and Trinidad beans, this blend produces a balanced yet unique profile with sweet and rather spicy overtones.
- **Bittersweet chocolate:** this product is mainly designed for use on very sweet and highly flavored cream centers as it produces very bitter coatings.
- **Semisweet cookie drop:** In order to have a good cocoa impact, it is recommended that the dominating West African beans be used in this product. The Brazilian and Sanchez

components' strong features compliment and contrast the West African component. In this application, a robust flavor is desirable for contrast in the baked cookies.[11]

Physical properties of chocolate

- Cocoa butter and cocoa powder are the most prevalent forms of chocolate,
- Producing in solid chocolate at room temperature that rapidly melts once inside the mouth.
- Because of its high melting point, -crystal form is commonly used in the manufacturing of chocolate.
- A smooth gloss, shine, and snap will come from a consistent crystal structure.
- The crystal form of chocolate is the most stable.
- As the temperature of cocoa butter rises, it transforms into a less stable form that melts below room temperature.
- In the polymorphic transformation theory of chocolate bloom, the benefits of these phenomena are used.
- With a pH of 6.8 to 8.1, processed (alkalized) cocoa powder is deeper in colour, ranging from brownish red to almost black.[12]

CHEMISTRY OF CHOCOLATE

Tryptophan is a brain molecule involved in the creation of serotonin, the neurotransmitter that causes elation. Phenyl ethylamine, a substance related to amphetamines that elevates blood pressure and blood glucose levels, is also found in chocolate. Those who feel more active as a result, a s well as a sense of well-being and pleasure. It is thought to act by inducing the production of b-endorphin, an opioid peptide that is responsible for the pleasurable effects. Phenyl ethylamine (caffeine tryptophan).[13]

MECHANISM

Cocoa is also a source of natural antioxidants, which are free radical freeloaders that protect cell membranes, DNA, and prevent plaque formation in artery walls by inhibiting the oxidation of low-density lipoprotein (LDL) cholesterol. The antioxidant activity of cocoa has been attached the procyanidins and their monomeric precursors, epicatechin, and catechin, which inhibit oxidation of LDL. Dark chocolate and cocoa inhibit LDL oxidation and increase high-density lipoprotein (HDL) cholesterol concentration. Catechin and epicatechin have been found in cocoa. Catechins are phytochemicals found in high amounts in a wide range of plant-based and liquor. Dark chocolate has a catechin concentration of 12mg/100mg.

Dark chocolate has 41.5 mg of epicatechin per 100 g. Consumption of catechin has been linked to a number of positive outcomes, including increased plasma antioxidant activity, bronchial artery dilatation, and reduced blood pressure. Fat oxidation and LDL oxidation protection Epicatechin appears to be a superior component in cocoa and other foods and beverages high in flavanols. In mammals and humans, it has been proven to improve endothelium function. Epicatechin reduces blood pressure and end-organ damage in salt-sensitive rat hypertension models.[14]

BENEFITS OF CHOCOLATE

Protection from Disease Causing Free Radicals: Free radicals are imbalanced molecules produced by biological activities in the body, particularly those that battle environmental contaminants we are exposed to on a regular basis. Antioxidants are substances that are thought to neutralise free radicals and protect the body from their harmful effects. Vitamins, minerals, and phytochemicals, which are beneficial plant compounds, are all antioxidants. Flavonoids and polyphenols are two types of antioxidants found in dark chocolate. The cocoa in dark chocolate has been revealed to have the highest concentration of polyphenols and flavonoids, surpassing even wine and tea. As a result, the higher the cocoa content of your next dark chocolate bar, the more antioxidants you'll get.

Potential cancer prevention: It may be difficult to believe, but that delicious dark chocolate you like may also help you avoid cancer. Dark chocolate's potential as a cancer-fighting food is one of its many advantages. Role of Dark Chocolate for the treatment of cancer is still under considerations by researchers.

Improved Heart Health: Flavonol is the most frequent flavonoid found in dark chocolate. According to the Cleveland Clinic, flavonol has a highly good effect on heart health by lowering blood pressure and boosting blood flow to both the heart and the brain. Dark chocolate flavonol can also assist blood platelets become less sticky and clot-resistant, lowering the risk of blood clots and stroke. Flavonol improves heart health by reducing blood pressure and increasing blood flow to both the heart and the brain, according to the Cleveland Clinic. Blood platelets become less sticky and clot-resistant as a result of dark chocolate flavonol, reducing the risk of blood clots and stroke.

Good For Overall Cholesterol Profile: Dark chocolate includes an equal proportion of oleic acid (a heart-healthy monounsaturated fat also found in olive oil), stearic, and palmitic acids

in its cocoa butter. The researchers discovered that just one week of dark chocolate consumption improved lipid profiles and reduced platelet reactivity in both men and women. Studies have also shown that:

- Consumption of polyphenol-rich dark chocolate enhanced HDL (good) cholesterol after three weeks.
- Consumption of polyphenol-rich dark chocolate for 15 days resulted in 6.5 percent and 7.5 percent reductions in total and LDL ("bad") cholesterol, respectively.
- LDL was reduced by 6% after seven days of frequent dark chocolate eating.
- Cholesterol, with an increase of 9% in HDL cholesterol.

Better Cognitive Function: Dark chocolate improve focus and memory in human. Acute as well as chronic ingestion of flavonol-rich cocoa is associated with enhanced blood flow to cerebral brain tissue, and it has been proposed that cocoa flavonol might be useful in disorders with reduced cerebral blood flow. It was also reviewed according that intake of flavonoid-rich foods, such as chocolate, wine, and tea, shows higher performance across multiple cognitive functions, and the correlations are dose dependent.

Blood Pressure and Blood Sugar Aid: A 2015 study compared the consumption of white chocolate by type 2 diabetics to high-cocoa polyphenol-rich dark chocolate by diabetics. For eight weeks, the participants consumed 25 g (just under one ounce) of black or white chocolate. Dark chocolate not only reduced hypertensive diabetics' blood pressure, but it also reduced fasting blood sugar levels, according to the researchers.

Antioxidant-Rich Super Food: Dark chocolate and cocoa powder were compared to super fruits including acacia, cranberry, blueberry, and pomegranate for total flavonol and polyphenol content, as well as antioxidant activity. Natural or non-alkalized cocoa has been used in the study's dark chocolates, cocoa powders, and cocoa liquid. This is significant since alkalinization of cocoa has been found to eliminate health benefits.[15]

Limitation and caution: It is necessary for chocolate consumers, especially those who consume an excessive amount of it, to know that chocolate remains a high-energy meal heavy in calories and sugar. The energy density of each 100 gm of chocolate is 2100 or 500 kcal, which is enough to contribute to weight gain, which is a risk factor for hypertension, diabetes, and cardiovascular and metabolic disorders in general. The information shown in flavor of chocolate consumption by this far-reaching study by Cambridge scholars is one of

association, not causation. More research is needed to verify that chocolate actually reduces the risk of heart attacks and strokes. The final seven studies chosen for meta-analysis were all done in the United States and Europe. As a result, extreme caution should be exercised when extending the findings to communities in other geographic areas or ethnic groups with genetic diversity. Applying the findings to other socioeconomic groups should be approached with caution. The findings confirm that the large amount of heterogeneity in the data they had to work with prevented them from estimating a dose response relationship between the amount of chocolate consumed and the degree of risk reduction in cardiovascular and metabolic outcomes in quantitative terms. The idea of creating a dose-response relationship in the feature, among other possibilities for examination that the field opens up, is an appealing research goal that can go a long way toward cementing chocolate's place as a meal that can provide dose-dependent positive effects.[12]

Medicated Chocolates

Medicated chocolates are made with a chocolate base and the drug is poured in so that the drug is incorporated into the chocolate and released from the chocolate. This is called to as a chocolate drug delivery system.[16]

There are four types of taste modalities, salty, sour, bitter, through the combination of these elements we can detect the “flavors” Childrens’ tastes sensation is much differed than adult infants and more over children prefer sweet-tasting substance.

Advantages

Chocolate has been demonstrated to stimulate in the synthesis of a substance known as "serotonin" in our bodies.

- It makes feel relaxed.
- Quick onset of action,
- Reduction in the drug dose of manufacture and scale,
- Increases drug loading capacity.

When some remedies have a bitter taste, oral delivery of bitter drugs causes patient noncompliance, especially in children. To solve this problem, a dose form that is most appropriate to pediatrics patients must be developed.[15]

Key Ingredients Used In Preparation of chocolate

Table 1: Key Ingredients Used In Preparation of chocolate.

Ingredients	Uses
Cocoa powder	Principal ingredients
Cocoa Butter	Solidifying agent
Lecithin	Emulsifier
Pharmaceutical grade sugar	Sweetening agent

METHOD OF PREPARATION [8]

All the ingredients are weighed accurately

↓

In a beaker, sugar and water is taken and sugar syrup is prepared on heating mantle.

↓

Cocoa butter is heated in a separate beaker, then the melt butter is poured into powder mixture and thoroughly combined to get a fine consistency.

↓

After that soya lecithin is added and mixed well.

↓

Finally the drug or API is added in prepared chocolate base.

↓

Then the flavoring agent is added before going to set in moulds

EVALUATION OF MEDICATED CHOCOLATE

A. Evaluation of chocolate base has following parameters

- **Taste, texture and mouth feel characteristics assessment:** Taste, texture & mouth feel characteristics of chocolate are evaluated by taking a panel of 10 human volunteers.[12]
- **Viscosity:** Brookfield Rotational digital viscometer is used to measure the viscosity (cps) of the prepared chocolate base. The spindle is rotated at 20rpm with the samples of chocolate base are heated at 50ºC before the measurement are taken.[12]

B. Evaluation Of Medicated Chocolates

General Appearance: The measurement of a number of variables such as chocolate's colour, presence or absence of an odour, flavour, surface texture, and physical imperfections are used to manage the overall look of a chocolate.[4]

Dimensions: The dimension of chocolate is measured by vernier's calipers.[4]

Blooming test

- **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.
- **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]

Moisture content determination: Moisture content is determination by using desiccators. The chocolates are keept in charged silica gel in desicator. After 24hrs, the formulation is taken out weighed and % Moisture Content is calculated by using formula.[5]

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

Drug content determination: Drug content of a medicated chocolate is determined by using U.V. spectrophotometer.[15]

In vitro drug release: The formulation is performed in USP dissolution apparatus types I (basket), using 0.1 N HCL as a dissolution media. The vessel of the dissolution apparatus filled with 900 ml of 0.1N HCL is placed and allowed to attain a temperature of 37±0.5ºC and 50rpm. Then chocolate formulations are placed in the basket. At predetermined time samples 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.[4]

Stability test: The stability studies of formulated formulations are 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.[4]

CONCLUSION

When most medications are bitter, oral delivery of these formulation results in patient noncompliance, particularly in children. To solve this restriction, it is suggested that a dosage

form be developed that is most suitable to pediatrics patients. Nowadays, most pharma companies are coming out with numerous alteration formulations such as dissolving tablets, dry syrups, lozenges, oral films, and so on, having this universal challenge of pediatrics in mind. In this review we tried to find formulation which can be best compatible with the pediatrics. As a chocolate provides formulations a smooth and creamy texture, and it's great for hiding the unpleasant flavors of some medication's excipients. Thus, it can be concluded that the chocolate formulations are attractive way to administer medications to patients via oral drug delivery.

REFERENCES

1. Prasanna JL, Ams BS, KR, MS, Kumar BA, Kumar AU. Formulation and evaluation of chocolates containing guaifenesin. European Journal Of Pharmaceutical And Medical Research, June 1, 2018; 5(7): 316.
2. Ithape PR, Ghadage PD, Gadhve JK, Mali AS. Oral drug delivery system challenges to pediatrics and current approaches. PharmaTutor., 2018; 6(6): 9-13.
3. Patel J, Joshi M, Thakkar V, Gohel M, Baldaniya L, Patel A. Medicated chocolate containing cefpodoxime proxetil: a novel solid dosage form for paediatric patient. In Proceedings of RK University's First International Conference on Research & Entrepreneurship (Jan. 5th & Jan. 6th, 2016) 2016.
4. Mayank S, Kumar JD. Chocolate formulation as drug delivery system for pediatrics. Indonesian Journal of Pharmacy, 2012; 23(4): 216-24.
5. Viswanath V, Narasimha RB, Purushothaman M, Sireesha S. Formulation and Evaluation of Fexofenadine Hydrochloride and Paracetamol Chocolate for Pediatrics. World Journal of Pharmaceutical Research, 2015; 4(9): 842-858.
6. Sonak S, Trivedi S, Wadher K, Umekar M. International Journal of Modern Pharmaceutical Research, 2019; 3(6): 104-109.
7. Naqvi RF, Khan A, Umer MF, Malik O, Shahwani NA. Design and Optimization of Novel Taste-Masked Medicated Chocolates of Dextromethorphan with In vitro and In vivo Taste Evaluation. Journal of Pharmaceutical Innovation, 2020; 1-5.
8. Pawar PD, Bakliwal AA, Talele SG, Jadhav AG. Formulation and evaluation of herbal chocolate as nervine tonic. Journal of Pharmaceutical Sciences and Research, 2019; 11(5): 1808-13.
9. Vasani C, Shah K. Preparation and evaluation of chocolate drug delivery system of albendazole. Research Journal of Pharmacy and Technology, 2016; 9(11): 1994-8.

10. Latif R. Chocolate/cocoa and human health: A Review. Neth J Med., Mar 1, 2013; 71(2): 63-8.
11. Patel ND, Shukla SK, Tomar P, Jain H, Pradhan p, Upadhyay U. Chocolate drug delivery system: a review. Indo American journal of pharmaceutical sciences, 2015; 2(6): 1077-1081.
12. Pawar PG, Darekar AB, Saudagar RB. Medicated Chocolate And Lollipops: A Novel Drug Delivery System For Pediatric Patient. Pharma Scie nce Monitor, 2018; 9(1).
13. Ackar D, ValekLendić K, Valek M, Šubarić D, Miličević B, Babić J, Nedić I. Cocoa polyphenols: can we consider cocoa and chocolate as potential functional food. Journal of chemistry, 2013; 1-7.
14. Haritha K, Kalyani L, Rao AL. Health benefits of dark chocolate. J. Adv. Deliv, 2014; 1: 184-94.
15. Chaudhari SA, Devare RR, Dewang PS, Patil VB, Patil AM, Pawar SP. Review: Chocolate Formulation As Drug Delivery System. Indian Journal of Drugs, 2018; 6(2): 136-141.
16. Sunil R, Mounika K, Shalini S, Venkatesham A. Design and fabrication of medicated chocolate formulation by chocolate drug delivery system. Journal of Current Pharma Research, 2016; 7(1): 2010-20.