

REVIEW: CHOCOLATE FORMULATION AS DRUG DELIVERY SYSTEM

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<p>*For Correspondence: P.S.G.V.P. M'S College of Pharmacy, Shahada-425409, Dist.-Nandurbar, Maharashtra.</p>	<p>ABSTRACT Chocolate/cocoa has been known for its good taste and proposed health effects for centuries. Most of the drugs are bitter due to which oral administration of these drugs leads to patient incompliance especially in children. To overcome this limitation, it is advisable to formulate dosage form, which is most acceptable for paediatric patients. Chocolate is one of the most palatable and favourite in children, so we have developed chocolate drug delivery system. Chocolate tastes good; it stimulates endorphin production, which gives a feeling of pleasure. It contains serotonin, which acts as an anti-depressant. It contains theobromine, caffeine and other substances, which are stimulants. Cocoa can also protect nerves from injury and inflammation, protect the skin from oxidative damage from UV radiation in topical preparations, and have beneficial effects on satiety, cognitive function, and mood. Medicated chocolate is prepared by using chocolate base and drug is incorporated to prepared chocolate base. The medicated chocolate can be evaluated for its appearance, moisture content, viscosity, blooming test, drug content determination and in vitro drug release. This review paper focused on health importance and usage of medicated as well as conventional chocolates.</p> <p>KEY WORDS: Medicated Chocolate, Cocoa, Paediatrics, Chocolate Formulation.</p>
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INTRODUCTION

Chocolate is highly sophisticated and much infinitely adaptable food that can be combined to create completely different taste and consistency sensations. Chocolate is an anhydrous medium resistant to microbial growth and hydrolysis for water-sensitive active agents. Chocolate abundantly contains compounds such as saturated fat, polyphenols, sterols, di and triterpenes, aliphatic alcohols, methylxanthines flavones, antioxidants Cocoa is the main ingredient of chocolate and it is loaded Chocolate in polyphenols. Chocolate containing the drug in suitable quantity is known as medicated chocolate. There are four types of taste modalities, salty, sour, bitter, sweet through the combination of these elements we can detect the "flavours" Children's tastes sensation is much differed than adult infants and more over children prefer sweet-tasting substance. Chocolate have been shown to help our body produce chemical known as "Serotonin". It makes feel relaxed. Further chocolate is also having some advantages like quick onset of action, reduction in the drug dose of manufacture and scale, increases drug loading capacity. Some drugs are bitter in taste due to which oral administration of bitter drugs leads to patient incompliance especially in children. To overcome this limitation, it is advisable to formulate dosage form, which is most acceptable for paediatric patients. Chocolate is one of the most palatable and favourite in children, so we have developed chocolate drug delivery system. Chocolate (in some regions also named bittersweet chocolate, semi-sweet chocolate, dark chocolate or "chocolate fondant") shall contain, on a dry

matter basis, not less than 35% total cocoa solids, of which not less than 18% shall be cocoa butter and not less than 14% fat-free cocoa solids.

TYPES OF CHOCOLATE

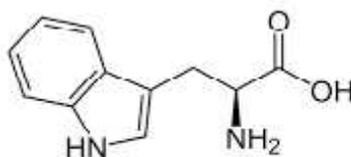
1. Sweet Chocolate- Sweet Chocolate shall contain, on a dry matter basis, not less than 30% total cocoa solids, of which at least 18% shall be cocoa butter and at least 12% fat-free cocoa solids.
2. Couverture Chocolate- Couverture Chocolate shall contain, on a dry matter basis, not less than 35% total cocoa solids of which not less than 31% shall be cocoa butter and not less than 2.5% of fat-free cocoa solids.
3. Milk Chocolate- Milk Chocolate shall contain, on a dry matter basis, not less than 25% cocoa solid (including a minimum of 2.5% fat-free cocoa solids) and a specified minimum of milk solids between 12% and 14% (including a minimum of milk fat between 2.5% and 3.5%).
4. Family Milk Chocolate - Family Milk Chocolate shall contain on a dry matter basis, not less than 20% cocoa solids (including a minimum of 2.5% fat-free cocoa solids) and not less than 20% milk solids (including a minimum of 5% milk fat). "Milk solids" refers to the addition of milk ingredients in their natural proportions.
5. Milk Chocolate Couverture -Milk Chocolate Couverture shall contain, on a dry matter basis, not less than 25% cocoa solids, not less than 14% milk, and a total fat of not less than 31%.
6. White chocolate -White Chocolate shall contain, on a dry matter basis, not less than 20% cocoa butter and not less than 14% milk solid.
7. Family Milk Chocolate -Family Milk Chocolate shall contain on a dry matter basis, not less than 20% cocoa solids (including a minimum of 2.5% fat-free cocoa solids) and not less than 20% milk solids (including a minimum of 5% milk fat). "Milk solids" refers to the addition of milk ingredients in their natural proportions.
8. Milk Chocolate Couverture -Milk Chocolate Couverture shall contain, on a dry matter basis, not less than 25% cocoa solids, not less than 14% milk, and a total fat of not less than 31%.

CHEMISTRY OF CHOCOLATE

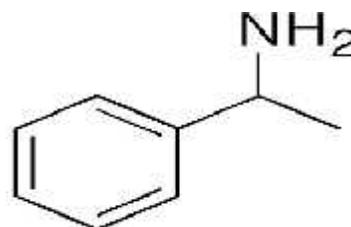
Phenyl ethylamine occurs naturally in the brain and is dubbed 'the love drug' due to its ability to produce feelings of well-being and contentment. It is also presented in significant concentrations in chocolate. Tryptophan are a chemical in the brain linked to the production of serotonin, the neurotransmitter that produces feelings of elation. Chocolate also contains Phenylethylamine, a chemical related to amphetamines and raises blood pressure and blood glucose levels. The results are that we feel more alert and give us a sense of well-being and contentment. It is believed to work by making the brain release b-endorphin, an opioid peptide that is the driving force behind the pleasurable effects.



Caffeine



tryptophan



Phenylethylamine

MECHANISM

Cocoa has been reported to be a source of natural antioxidants, the free radicals' scavengers that preserve cell membranes, protect DNA, prevent the oxidation of low-density lipoprotein (LDL) cholesterol that leads to atherosclerosis and prevent plaque formation in arterial walls. The antioxidant activity of cocoa has been attributed to 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 concentrations. Catechins are phytochemical compounds found in high concentrations in a variety of plant-based foods and beverages. The catechin content in dark chocolate is 12mg/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 oxidation. Epicatechin seems to be a major bioactive constituent of cocoa and other flavonol-rich foods and beverages. It has been shown to improve endothelial function in animals and humans. In salt sensitive 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.

Method of Preparation

1. Preparation of chocolate base- The sugar syrup is initially prepared by heating sugar (pharmaceutical grade) and water in a beaker using heating mantle at 50C for 4-5 minutes. The cocoa base is prepared by melting the cocoa butter in a beaker for 2 minutes and adding the above prepared sugar syrup and cocoa powder to it. This mixture is cooled up to semisolid consistency and adding a flavouring agent.

- Method of preparation of chocolate-

Oven was set at 50^C. Then prepared chocolate base was melted until it becomes a free-flowing liquid. After that, required quantity of Active pharmaceutical ingredients was added. Then it was stirred well with the help of magnetic stirring for 10 minutes to ensure uniform mixing. Then we poured the above mixture in a polycarbonate set mould and cooled for 15 minutes until it become solid.

2) Preparation of chocolate base-

Chocolate were formulated with total fat of 25-35% (w/w) from cocoa liquor and cocoa butter with more than 34% total cocoa.

- Method of preparation

Oven was set to 50C. In beaker, sugar and water was taken and kept in the oven for 4-5 min and syrup was prepared. Then cocoa butter was taken and kept in the beaker in the oven for 1 min. Then sugar syrup was removed from the oven, and cocoa powder was 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 was cooled up to semisolid consistency and then flavour was added.

BENEFITS OF CHOCOLATE

1. Protection from Disease Causing Free Radicals: -Free radicals are unbalanced compounds created by cellular processes in the body, especially those that fight against environmental toxins we are exposed to on a daily basis. Antioxidants are the compounds that are believed to neutralize free radicals and protect the body from their damage. Antioxidants include vitamins, minerals and phytochemicals — helpful plant compounds. Two groups of antioxidants prevalent in dark chocolate are flavonoids and polyphenols. Dark chocolate's cocoa has actually been shown to have the highest content of polyphenols and flavonoids, even greater than wine and tea. So, the higher the

cacao/cocoa percentage of your next dark chocolate bar, the more awesome antioxidants you will consume.

2. Potential Cancer Prevention: -It may be hard to believe, but that tasty dark chocolate you eat and love may also help you ward off cancer. That is right — one of the benefits of dark chocolate is its potential as a cancer-fighting food. According to the American Cancer Institute: “Given chocolate’s rich supply of flavonoids, researchers have also investigated whether it may play a role in cancer prevention. The studies in cancer prevention are still emerging.”

3. Improved Heart Health: - Flavonols are the main type of flavonoid found in dark chocolate. According to Cleveland Clinic, research has shown that flavonols have a very positive effect on heart health by helping lower blood pressure and improving blood flow to the heart as well as the brain. Dark chocolate flavonols can also help make blood platelets less sticky and able to clot, which reduces the risk of blood clots and stroke. A study published in International Journal of Cardiology had subjects either consume a daily dose of flavonoid-rich dark chocolate or non-flavonoid white chocolate for two weeks. The results showed that flavonoid-rich dark chocolate intake significantly improved heart circulation in healthy adults. On the other hand, white chocolate with zero flavonoids to brag about had no positive health effects on the subjects.

4. Good for Overall Cholesterol Profile: -The cocoa butter found in dark chocolate contains equal amounts of oleic acid (a heart-healthy monounsaturated fat also found in olive oil), stearic and palmitic acids. The researchers found that just one week of dark chocolate consumption improved lipid profiles and decreased platelet reactivity for both men and women while reducing inflammation only in women.

Studies have also shown that:

- Dark chocolate’s cocoa polyphenols may be involved in cholesterol control.
- Three-week consumption of polyphenol-rich dark chocolate increased HDL (good) cholesterol.
- 15-day consumption of polyphenol-rich dark chocolate resulted in total and LDL (“bad”) cholesterol decreases of 6.5 percent and 7.5 percent, respectively.
- Seven-day consumption of regular dark chocolate resulted in a 6 percent decrease of LDL cholesterol and a 9 percent increase of HDL cholesterol.

5. Better Cognitive Function: - Dark chocolate makes my list of 15 brain foods to boost focus and memory for good reason. Previous research showed that “acute as well as chronic ingestion of flavonol-rich cocoa is associated with increased blood flow to cerebral gray matter and it has been suggested that dementia and stroke cocoa flavonol might be beneficial in conditions with reduced cerebral blood flow, including.” The study concludes that “intake of flavonoid-rich food, including chocolate, wine, and tea, is associated with better performance across several cognitive abilities and that the associations are dose dependent.”

6. Blood Pressure and Blood Sugar Aid: - A study published in 2015 compared type 2 diabetics’ consumption of white chocolate versus high –cocoa polyphenol-rich dark chocolate. The subjects consumed 25 grams (a little under one ounce) of dark or white chocolate for eight weeks. The researchers found that not only did dark chocolate lower the blood pressure of the hypertensive diabetics, but it also decreased fasting blood sugar.

7. Antioxidant-Rich Super food: -The total flavonol and polyphenol content as well as antioxidant activity content of dark chocolate and cocoa powder were compared to super fruits like acai, cranberry, blueberry and pomegranate. The dark chocolates, cocoa powders and cocoa beverage in the study all contained natural or non-alkalized cocoa. This is important to note since the alkalisation of cocoa has been shown to destroy healthy polyphenol compounds.

EVALUTION OF CHOCOLATE

1) Evaluation of chocolate base:

- Viscosity determination of chocolate base- Brookfield Rotational digital viscometer (DV I+) was used to measure the viscosity (in cps) of the prepared chocolate base. The spindle (LV1) was rotated at 20rpm; Samples of chocolate base were heated at 50°C before the measurements were taken.
- Taste, texture and mouth feel characteristics assessment -Taste, texture & mouth feel characteristics of chocolate were evaluated by taking panel of 10 human volunteers.

2) Evaluation of Medicated chocolates

1. 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 colour, presence or absence of an odour, taste, surface texture and physical flaws.
2. Dimensions - Vernier’s callipers measured the dimension of chocolate.
3. Moisture content determination- Moisture content of chocolate formulation is determined by using Digital Karl Fischer Titrato model Vee go/Matic. These instruments are designed to calculate percentage (%) water content by using formula:

$$(\%) \text{ Water} = \frac{[\text{Volume (mL) TS of water determination consumed} \times f \text{ (mg/m)}] \times 100}{\text{Weight of sample (mg)}}$$

Where, f = the number of mg of water (H₂O) corresponding to 1mL of water Determination TS,
TS= water determination test sample

4. Blooming test-

A) Fat Bloom: When a thin layer of fat crystals forms on the surface of the chocolate formulation. This will cause the chocolate to lose its gloss and a soft white layer will appear, giving the finished article an unappetizing look. Fat bloom is caused by the recrystallization of the fats and/or a migration of a 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 caused by condensation (when the chocolate is taken out of the refrigerator). This moisture will dissolve the sugar in the chocolate. When the water evaporates afterwards, the sugar recrystallizes into rough, irregular crystals on the surface. This gives the chocolate an unpleasant look. Each sample was subjected to treatment cycles comprised (1) 30°C for 11 hours, (2) temperature shifting for 1 hour, (3) 18°C for 11 hours, and (4) temperature shifting for 1 hour. A test chocolate formulation observed, after the step at 18°C for 11 hours, whether blooming has taken place.

5. Drug-excipients interaction study- Differential scanning calorimeter Drug–Excipient interaction study was performed by Differential scanning calorimeter was performed.
6. Physical observation -This study was performed to determine any interaction or physical changes that may occur when kept with various excipients at different environmental conditions. Drug was mixed with various excipients in the ratio of 1:5 and was kept in closed vials. These vials were placed at 25°C for 1 month. The vials kept at 28°C were considered control samples. After one-month interval, sample vials were withdrawn from each test group and physical appearance and drug degradation was observed.
7. Drug content determination- Drug content of a medicated chocolate was determined by using UV Spectrometer. In vitro drug release study of Chocolate formulation was performed in USP

dissolution apparatus Type 1 (Basket), using suitable dissolution media. The bowls of the dissolution tester was filled with 900mL of suitable drug was placed and allowed to attain a temperature of $37\pm 0.5^{\circ}\text{C}$ and 50rpm. A chocolate formulation was placed in the basket. At predetermined time interval i.e. 1, 2, 3, up to 10 minutes, 10mL sample was withdrawn and volume was replaced with equal quantity of fresh medium. The collected samples were filtered and analyzed by UV Spectroscopy the concentration of drug was calculated using slope of calibration curve and cumulative percentage release was calculated.

8. Stability of medicinal products may be defined, as the capability of a particular formulation in a specific container to remain within its physical, chemical, microbial, therapeutic and toxicological specification, i.e. stability of drug is its ability to resist deterioration. 90% of labelled potency is generally recognized as the minimum acceptable potency level. Deterioration of drug may take several forms arising from changes in physical, chemical and microbiological properties. The changes may affect the therapeutic value of preparation or increase its toxicity
9. Viscosity-Shear rate is the single most important control parameter for viscosity evaluation of chocolate. Viscosity behaviour for chocolate formulations typically shows a decrease as the shear rate increases. This type of flow performance is referred to as 'shear thinning' and has been given the scientific word 'pseudo plastic'. Depending on the combination of ingredients and other additives in each batch of chocolate, the degree of shear thinning behavior can vary substantially. Therefore, monitoring performance by making viscosity measurements in Quality Control is a most necessary control procedure.
10. Hardness-Firstly, hardness can be defined and calculated from penetrometer measurements. Soeters described this relationship as: $H (\text{kg/cm}) = 15.069 * 100/p$

Where, p is the penetration in mm/10 (using a 9.18-degree cone with a blunted tip, 0.15cm diameter and a total weight of 100g).

The hardness of a chocolate or compound coating is an expression of its structure and solidity. Since it is the fat phase of such products that defines the structure, it might be expected that the chocolate hardness will be related to the structure and solidity of the fat phase.

CONCLUSION

From above study, we concluded that the chocolate provides smooth and creamy texture to formulation and are excellent for taste masking unpleasant flavours associated with some drugs and other excipients. The chocolate formulation provides a palatable means for delivering medicaments through oral drug delivery.

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