MEDICATED CHOCOLATE AND LOLLIPOPS: A NOVEL DRUG DELIVERY SYSTEM FOR PEDIATRIC PATIENT

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ABSTRACT
Medicated chocolate and medicated lollipops are more acceptable dosage form in pediatrics because conventional dosage forms like tablet and capsule have some limitations in case of pediatric patients for example bitterness of tablet and they can’t swallow the conventional dosage form. To overcome those problems new drug delivery system has been developed by the Researchers i.e. Chocolate drug delivery system (medicated chocolate) and medicated lollipops. This type of system increases aesthetic appeal which indirectly increases the patient compliance. Medicated chocolate and medicated lollipops contains a sweetening agent, flavoring agent, and coloring agent that more to attract the pediatrics. The advantages of the medicated chocolate and lollipops are taste masking of bitter drugs, enhanced bioavailability, enhanced the retention time of the dosage form in the oral cavity which also overcomes gastric irritation. Mostly disadvantages of the chocolate have been focused but those are some health benefit of a chocolate exists too like antioxidant property, reduction in cardiovascular and metabolic disorder and so on which are used by chocolate drug delivery system. Chocolate drug delivery system is not only beneficial for the pediatric patient but also for the geriatric patient. The patients with diabetic conditions can also enjoy the chocolate drug delivery system by the medications which consist of dark chocolate. Cocoa obtained from the natural source there are minimum side effects of the chocolate drug delivery. The antimicrobial agent is the most incorporated in lollipop formulation. Most of the medicated lollipops are available in the market for the treatment of cold and cough.

KEYWORDS: Patient compliance, medicated chocolate, pediatric patient, medicated lollipops, novel drug delivery.

INTRODUCTION
Medicated chocolate:
Chocolate is made from cocoa beans, dried and fermented seeds of the cocoa tree (theobroma cacao). The scientific name theobroma means “food of the goods” from (theos), meaning “god”, and (broma), and meaning “food”. Chocolate is a typically sweet, usually brown food preparation of coca, seeds, roasted and ground. It is made in the form of a liquid, paste or in a block, or its use as a flavoring agent in other foods. Chocolate may contain cocoa solids and cocoa butter in varying properties. Cocoa solids are a source of flavonoids. Such as theobromine, phenethyllamine, caffeine, chocolate also contains anandamide. They have been consumed by
humans since at least around 500 AD. Dark chocolate is one such food that historically used for healing purposes. The chocolate consumption ranges from 120g per person per year in China to around 12000g per person per year in Iceland. The use is in the middle of this range, with consumption of approximately 500g per person per year. [2] Chocolate is highly advanced and much infinitely adaptable food that can be combined to create completely different taste. Chocolate is an anhydrous medium resistance to microbial growth and hydrolysis for water-sensitive active agent. [3] There are several type of chocolate according to the proportion of cocoa used in particular formulation like dark chocolate, milk chocolate, cocoa powder or bittersweet chocolate. [4]

Medicated chocolate is prepared by using chocolate base and the drug is incorporated into the prepared chocolate base. As the drug is incorporated into the chocolate and the drug is released from the chocolate, it is called as chocolate drug delivery system has advantages that include a possible bypass of first-pass effect and avoidance of pre-systemic elimination within the GI tract. Chocolate is also an anhydrous medium and is therefore to microbial growth and to hydrolysis of water-sensitive active agents. Chocolate is well-suited as a vehicle for delivering active agents in many aspects. [5] The dark chocolate also know as black chocolate or plain chocolate which is produced by adding fate and sugar to cocoa, and contains a higher percentage of cocoa. It is chocolate with no milk or very less than milk chocolate. [6]

The modern discovery of biologically active phenolic compounds (consisting of α–OH bounded to aromatic hydrocarbon group) in cocoa have changed this perception and stimulated research on its effects in again, oxidative stress, regulate blood pressure, and atherosclerosis. Chocolate came to Europe in the 16th century. Since then, the modern chocolate production industry has developed, and cocoa seeds are now prepared in different ways. Initially it was thought of as a luxury item, but currently, it is considered to be a medicine. [7]

**Medicated lollipop:**

Lollipops are solid dosage forms, containing the medicament in a sweetened & flavored base, intended to dissolve slowly in the mouth. Lollipops have mainly contained the additives like sweetening agent, flavoring agent, the coloring agent, opacifiers & stabilizing agent. Medicated lollipop are the flavored medicated dosage forms designed to be sucked and held in the mouth or pharynx containing one are or more active pharmaceutical ingredient usually in the sweetened base lollipops are designed to reduce oropharyngeal symptoms, which are commonly caused by local infection and also for systemic effect provided the drug is well absorbed through the buccal lining when it is swallowed. Medicated lollipops are used for pediatric patients because they
cannot swallow conventional oral dosage forms. Medicated lollipops are prepared to release medicines slowly to yield a constant level of drug in the oral cavity or to soak the throat tissue in solution of the drug. Drug usually incorporated into lollipop include antimicrobials, analgesics, antidepressants, anesthetics, antiseptic, anti-tussives, corticosteroids, aromatics, astringents, decongestants, and demulcents. However, that is by no means as exhaustive list as many other drugs may allow themselves to delivery by a lollipop. As well, both individual and multi-ingredient lollipops can be prepared, depending on the particular patient’s needs, depending on the types of lollipops. They may be prepared by molding or by compression. [8]

Medicated lollipops are a small, medicated candy designed to be disappeared slowly in the mouth to lubricant and so that irritated tissue of the throat. A small flavored tablet made sugar or syrup or often medicated. The small medicinal tablet originally in the shape of lollipops taken for a sore throat and that dissolved in the mouth. Lollipops are large sugar boiled confectionary of various flavored attached to a plastic stick which can be consumed over a long period of time through licking. The plastic stick is used to hold the attachment together. Medicated lollipops are the solid dosage forms that dissolved slowly in the mouth and they can be easily swallowed are increasing popularity, especially among pediatric patients medicated lollipops are solid unit dosage form of the medicament which is still in commercial production. Most of the lollipops preparations are available as over the counter medications. This dosage forms can be utilized for local as well as a wide range of active ingredients can be incorporated inside them. Medicated lollipops are most commonly used for utilized effect in the mouth. They can also be used for systemic effects if the drug is well absorbed through the buccal lining or is swallowed newer drugs. [9]

**History of chocolate:**

Chocolate originated from Mexico where the Mayas, Incas and Aztecs cultivated the cocoa tree. At first, it was seen as aphrodisiac, accessible only to the affluent and rich. Because of the high price, chocolate was replaced by coffee and tea as the main drink. Nowadays cocoa is grown mainly in West Africa, Indonesia, or Sri Lanka. In the paste, due to its health effects, it was considered the drink of goods. An association that gave rise to the scientific name of the cocoa tree, *theobroma cocoa*, from the Greek words *theo* (god) and *broma* (drink) the attribution was provides to the tree by a Swedish naturalist Carl Von Linne (1707-1778). In fact, this name is symbolic of the social, and religious, and economical importance chocolate in both new or old world cultures. [7]
Types of chocolates:
The different forms and flavors of chocolate are produced by various quantities of the different ingredient. Other flavors can be obtained by different time and temperature when roasting the beans.

A. Milk chocolate: this is solid chocolate made with milk, in the form of condensed milk, milk solid and liquid milk was added. In 1875, Swiss confectioner Daniel peter, in cooperation with its neighbor Henri Nestle in Vevey, developed the first solid milk chocolate using milk solid or condensed milk.

B. 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

C. White chocolate: this is made of sugar, milk, or cocoa butter, without the cocoa solids. It usually consists of cocoa butter, sugar, or milk solid and is characterized by a pale yellow. White chocolate may include additional flavoring. Vanilla, strawberries a natural additive.

D. Cocoa powder: “cocoa powder” is most of the time used in baking. That also use for drinking with added milk and sugar. There are two varieties of unsweetened cocoa powder one is a natural cocoa (like the short the produce by the broma process), and another is a Dutch-process cocoa. The Dutch processing split most of the flavonoids present in cocoa. In 2005 Hershey terminated their pure Dutch-process European style cocoa and replaced it with special dark, blend of natural and Dutch-process cocoa.

E. Unsweetened chocolate: they also called as bitter or cooking chocolate. It is pure chocolate liquor mixed with some from fat to develop a solid substance. The pure, ground, roasted cocoa beans impart a strong, deep chocolate flavor. With the extra sugar added, however it is used as the base for the cakes, brownies, confection, and cookies.

F. Bittersweet chocolate: “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.
G. Semisweet chocolate: Semisweet chocolate does not contain milk solid. It is a dark chocolate with (by definition in Swiss usage) half as much sugar as cocoa, beyond which it is "sweet chocolate". [4]

Physical properties of chocolate:

♦ The most common form of chocolate is cocoa butter and cocoa powder. Cocoa has a melting point of around 34-30°C (93-101°F).
♦ Rendering solid chocolate at room temperature that readily melts once inside the mouth.
♦ Cocoa butter display polymorphism, α having 17°C melting point, γ having melting point 23 ºC, β having melting point 26°C and β crystal having in melting point 35-37°C.
♦ To the production of chocolate, typically β-crystal form is use, because of its high melting point.
♦ A uniform crystal structure will result in a smooth texture, shine and snap.
♦ Increase in a temperature of cocoa butter changes the structure to a less stable form, which melts below room temperature.
♦ The β crystal form of chocolate is most stable.
♦ The advantages are taken of this phenomenon in the polymorphic transformation theory of chocolate bloom.
♦ The refractive index of cocoa butter is near about 1.44556 to 1.44573.
♦ The iodine value of cocoa butter is 32.11 to 35.12.35.57.
♦ The acid value of cocoa butter is 1.68.
♦ Saponification value is 191.214, 192.88 to 196.29 [10]
♦ Natural cocoa powder has a light brown color and an extractable pH is 3.5 to 5.8.
♦ The processed (alkalized) cocoa powder is darker in color, ranging from brownish red to nearly black, with a pH from 6.8 to 8.1 [11]

Chemistry:

♦ The pharmacologically active ingredients of cocoa seeds include alkaloids, theobromine (0.5% to 2.7%), amines, theophylline, caffeine (approximately 0.25% in cocoa), fatty acids, triamine, trigonelline, Magnesium, polyphenols (including flavoring), phenythyamine, and n-acyl ethanolamines.
A conventional chocolate bar (40 to 50 g) contains theobromine (86 to 240 mg) and caffeine (9 to 31 mg). The characteristically bitter taste of cocoa is produced by the reaction of diketopiperazines with theobromine while roasting.

Theobromine is produced commercially from cocoa husks. Cocoa butter contains triglyceride fatty acids consisting mainly of oleic acid, stearic acid and palmitic acids.

It also contains myristic, arachidic, lauric, palmitic, linoleic, and α-linolenic acids. Cocoa is rich in polyphenols that have beneficial effects on cardiovascular disease.

In cocoa, the polyphenols are appropriate attention is flavanols, a subclass of flavonoids, which are in changes a subclass of polyphenols.

Cocoa is more than 10% flavanol by weight. Flavanols can be monomeric in cocoa beans these are mainly (-)-epicatechin and (+) catechin, dimeric (consisting of 2 units of epicatechin with differing linkages) or polymeric (combination of monomers and chains of up to 10 units or more have been found).

Mechanism:

Cocoa is reported to be a source of natural antioxidants, the free radical freeloaders that protect cell membranes, protect DNA, inhibit the oxidation of low-density lipoprotein (LDL) cholesterol that manages to atherosclerosis and prevents plaque development in arterial walls. 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 phytochemical compounds detected in high densities in a mixture of plant-based and liquors. The catechin content in dark chocolate is 12mg/100mg. The epicatechin content in dark chocolate is 41.5mg/100gm. The consumption of catechin has been correlated with a variety of advantageous outcomes including enhanced plasma antioxidant activity, bronchial artery dilation, fat oxidation and protection of LDL oxidation.

Epicatechin seems to be a superior ingredient of cocoa and another flavanols-rich foods and liquors. It is has been shown to enhance endothelial function in mammals and humans. In salt-sensitive mammal models of hypertension, epicatechin lowers blood pressure and the associated end-organ damage. The nitric oxide seems to play an important role in the protection of both hypertension and endothelial dysfunction. The antioxidant capability of dark chocolate is 13.1 per 100g. [13]
Benefits of chocolate:

Dark chocolate has recently been discovered to have a number of health benefits. The various health benefits of dark chocolate include, alleviation of cardiovascular disease, protection against the heart disease, stroke prevention, improvement in hypertension (high blood pressure), regulation of blood sugar and insulin dependence, reduce risk of types ii diabetes, antioxidant protection, alleviation of old and cough, reduced cancer risk, reduce risk of colon cancer, slowing aging, increased immune function, showing the progression of aids, DNA repair and protection, Alzheimer protection, improvement of premenstrual syndrome, prevention of alopecia.

1. **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.

2. **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.

3. **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.

4. **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.
5. **For brain:** dark chocolate increases blood flow to the brain as well as to the heart, so it can be helpful to improve cognitive function. Dark chocolate contains several chemical compounds that have a stimulate action and positive effect on the mood and cognitive health. Chocolate contains phenyl-ethylamine (PEA) and PEA encourages the brain to release endorphin and feel alert. Dark chocolate also contains caffeine, a mild stimulate. However, dark chocolate contains much less caffeine than coffee and hence ingredients of chocolate were used in mood disorder.

6. **For oral hygiene:** dark chocolate contains theobromine, which has been show to curve tooth enamel. That means that dark chocolate lowers the risk of getting decays in decent dental hygiene. Theobromine is also a mild stimulate, though not as strong as caffeine. It can help to overcome cough. Theobromine works by suppressing the activity of the Vagus nerve, which causes coughing and curves a cough.[13]

7. **Rich source of antioxidants:** oxidative stress and reduce antioxidant defense play key role in the pathogenesis of atherosclerosis. Chocolate is the third highest daily source of antioxidants for Americans. Antioxidants found in chocolate have been shown to inhibit plasma lipid oxidation. However, there is a study retracting the direct antioxidant potential of chocolate, documenting that the large increment in plasma total antioxidative capability observed later that the consumption flavans-rich food is most likely not due to flavanols but reasonable is a consequence of the increased uric acid level resulting from fructose metabolism.

8. **Antidiabetic effects:** numerous approaches have been tried improve insulin sensitivity in diabetics. Insulin sensitivity partially relies on nitric oxide bioavailability in endothelial cells; hence flavanols may reduce insulin resistance by ameliorating no bioavailability. A reduction in insulin resistance in insulin sensitivity was observed after ingestion flavanol-rich chocolate in healthy subject and hypertension patients. Another study demonstrated a positive impact on glucose and insulin response to an oral glucose tolerance test, in hypertension adults with impaired glucose tolerance following flavanol-rich chocolate ingestion.

9. **Anti-obese effects:** obesity is one of the major risk factor in the development of CVD. In a study, an identical high fat diet, with or without cocoa, was fed to rats for three weeks, cocoa consumption led to a significant decrease in total body weight, mesenteric white adipose tissue weight, and serum triglycerides. When DNA analysis was carried out on the liver and mesenteric fat tissue sample, the result showed a reduction in expression for various
genes associated with fatty acid transport and synthesis in liver and mesenteric fat and increased expression of genes associated with thermogenesis.

10. Antitumor effects: a few in vitro studies suggest cocoa inhibits the growth of cancerous cells. The exact anticancer mechanism is not clearly understood at this stage. On the other hand, some studies suggest that excess chocolate intake makes a person more prone to develop cancers. Further pre-clinical and clinical trial are needed to investigate the mechanism involved in cocoa action and to justify cocoa’s usage as a therapy for the prevention and treatment of cancer.

11. Anti-inflammatory effects: chocolate inhibits lipoxygenase pathways, by directly binding to the active sites of the enzymes lipoxygenases. [7, 13]

Limitation and caution:

It is very important for the chocolate consumer particularly those who eat excess amount of it, to aware that chocolate continue to be high-energy food rich in calories and sugar content. The each 100 gram of chocolate contains energy density of 2100 KJ or 500 kilocalories is high enough to contribute to weight grains, which in itself is a risk factor for hypertension, for diabetes and for cardiovascular and metabolic disorder in general.

The evidence presented by this far-reaching study by Cambridge researchers in favor of chocolate consumption is one of association, and or not of causation. Further studies would be required to prove that chocolate actually causes marked reduction in the incidence of heart attacks and stroke.

The seven studies that were finally selected for meta-analysis had been conducted in the United States and Europe. Therefore caution should be exercise in generalizing the finding and extrapolating them to population in other geographic locations, or to ethnic group that’s genetically diverse. Generalizing the finding to other socioeconomic group should also be handled cautiously.

The authors recognize that the considerable heterogeneity in the data they had to deal with prevented them from attempting to estimate a dose response relationship between the amount of chocolate and its effect in quantitative terms on the degree of risk reduction in cardiovascular and metabolic outcomes.

Among other avenues for investigation that the field unfurls, the possibility of developing a dose-response relationship sometimes in the feature is an attractive research goal that can go a long way in consolidating the position of chocolate closer to the category of a food that can be providing dose-dependent beneficial effects. Does adjustment of chocolate could conceivably be
one of the ways to manage the calorific input in the event that chocolate was consumed for the health of benefit.

Notwithstanding the limitation and cautionary not listed above, it would be reasonable for prevention of cardiovascular and metabolic disorder. \[14\]

**Chocolate manufacturing progresses:**

Chocolate manufacturing processes generally share common features (figures) such as:

1. Mixing
2. Refining
3. Conching of chocolate paste
4. Tempering and depositing
5. Moulding and demoulding \[15\]

![Flow chart of chocolate manufacture](image)

**Methodology:**

**Preparation of chocolate base:** The sugar syrup is initially prepared by heating sugar (pharmaceutical grade) and water in a beaker using heating mantle at 50°C 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 chilled up to semisolid consistency and adding a flavoring agent.
**Method preparation of chocolate:** Oven was set at 50°C, 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 uniform mixing. Then we poured the above mixture in a polycarbonate set mould and cooled for 15 minutes still it becomes solid. [16]

**Formulation of medicated chocolate:** Prepared chocolate squares containing drug in appropriate quantity is known as medicated chocolate. [5]

**Evaluation of chocolate:**

**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 with the samples of chocolate base are heated at 50°C before the measurement are taken.

**Taste, texture, and mouthfeel characteristics assessment:** Taste, texture & mouthfeel characteristics of chocolate are evaluated by taking a panel of 10 human volunteers on a rotating scale of 1-5 (table 1).

**Table 1: taste, texture and mouth feel characteristics assessment**

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Characters</th>
<th>Criteria</th>
<th>Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Appearance</td>
<td>Glossy, even shine; no streaks, dots, cracks or “fog”</td>
<td>1-5 with 5 being the best</td>
</tr>
<tr>
<td>2</td>
<td>Aroma or small</td>
<td>Chocolaty with only a light scent of any flavorings; fresh with no burnt, smoky, chemical smells.</td>
<td>1-5 with 5 being the best</td>
</tr>
<tr>
<td>3</td>
<td>Snap</td>
<td>Break clean without crumbling or flavoring; ideally a crisp pop when broken (loudest for dark chocolate)</td>
<td>1-5 with 5 being the best</td>
</tr>
<tr>
<td>4</td>
<td>Taste</td>
<td>Chocolaty flavours not overpower the chocolate taste. Good aftertaste</td>
<td>1-5 with 5 being the best</td>
</tr>
<tr>
<td>5</td>
<td>Texture</td>
<td>Creamy and smooth, not waxy; promptly and evenly melts in mouth.</td>
<td>1-5 with 5 being the best</td>
</tr>
</tbody>
</table>

**Evaluation of medicated chocolate**

**General appearance:** the general appearance of a chocolate formulation, its visual identity and overall “elegance,” essential (i) for consumer acceptance, (ii) for control of lot to lot uniformity and (ii) for monitoring trouble-free manufacturing. The control of the general appearance of a chocolate involves the measurement of a number of attribute such as a color of chocolate, presence or absence of an odor, taste, surface texture and physical flaws.

**Dimension:** the dimension of chocolate was measured by vernier’s caliper.
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,

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

Where,

F=the number of mg of water (H$_2$O) corresponding to 1ml of water determination TS,

TS=water determination test sample.

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.

In vitro drug release:

In vitro drug release study of chocolate, 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±0.5°C and 50rpm. Then chocolate formulation is placed in the basket. At predetermined time 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.

Stability test: It is the responsibilities of the manufactures 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 deterioration. 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.

**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(°C/RH) and 2-8°C 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. [17]

**Medicated lollipops:**

**History of lollipops:** the idea of an edible candy on stick is very simple, and it is probable that the lollipops has been invented and reinvented numerous times. The first confectioneries that closely resemble what we call lollipops date to the middle ages, when the nobility would often eat boiled sugar with the aid of stick or handles.

The invention of the modern lollipops is still something of mystery but a number of American companies in the early 20th century have laid claim to it. According to the book *food for thought: extraordinary little chronicles of the world*, they were invented by George smith of New Haven, Connecticut, who started making large boiled sweet mounted on stick in 1908. he named them after a racehorse of the time, lolly pop and trademarked the lollipop name in 1931.

The term ‘lollipop’ was recorded by English lexicographer Francis Grose in 1796. The term derived from the term “lolly” means tongue and “pop” mean slap. The first references to the lollipop in its modern context date to the 1920. Alternatively, it may be a word of Romany origin being related to the Roma tradition of selling toffee apples sold on stick. *Red apple* in the Romany language is *loli phaba.* [18]

**Types of lollipops:**

**Hard lollipops:** Hard lollipops might be recognized solid syrups of sugars. These dosage forms are made by heating sugar and other ingredients together and then pour the mixture into a mold. Hard lollipop is similar to hard candy. In fact, many hard lollipop formulas are modifications of hard candy formulas. The dosage form needs low moisture content. So water is evaporated by boiling the sugar mixture during the compound process. Hard candy lollipop is mixture of sugar and other carbohydrate in an amorphous or glassy condition. These lollipops can be considered
solid syrups of sugar and usually have a moisture content of 0.5% to 1.5%. Hard lollipops should not disintegrate but instead provide a slow, uniform dissolution (or) erosion over 30 minutes.

**Soft lollipops:** Soft lollipops have become popular because of the ease with which they can be extemporaneously prepared and their applicability to a wide variety of drugs. The base usually consists of a mixture of various, acacia, or similar material; glycerol, gelatin or acacia: sources base. These lollipops may be colored and flavored and they can be either slowly dissolved in the mouth or chewed, depending on the intended effect of the incorporated drug. [9]

**Advantages of medicated lollipops:**

- Keeping the drug in contact with the oral cavity for an extended period of time
- Having formula that are easy to changes and can patient specific.
- Lollipops can be given to those patients who have difficulty in swallowing.
- Lollipops have pleasant taste and it extend the time that a quantity of drug remains in the oral cavity to produce a therapeutic effect also a pharmacist can prepare lollipop extemporaneously with minimal equipment and time.
- Lollipop extend time of drug in the oral cavity to to elicit a specific effect
- Lollipops are easy to prepare for minimum amount of equipment and time
- Do not require water intake for administration. The technique is noninvasive and it is case with parenteral.

**Disadvantages of medicated lollipops:**

- Heat labile drug cannot use in this formulation because of the high temperature required for preparation.
- Drug having minimum bitter taste are suitable.
- Heat stable drug are suitable. [19]

**General consideration for designing medicated lollipops:** Since the development cost of a new chemical entity is very high, the pharmaceutical companies are now focusing on the development of new drug delivery systems for existing drug with an improved efficiency and bioavailability together with reduced dosing frequency to minimize side effects, typically, oral candidacies takes the form of an adherent white, curd-like, circumscribed plaque anywhere within the oral cavity. There are many drugs dosage forms like lozenges, tablets, inhalers, or syrups, are in market for the treatment of the same. These preparations are commonly used for the purpose of local effect or systemic effect. New drug design to this area always benefit for the patient, physician and
drug industry. There several dosages from like in the market but there is a need for more dosage forms which acts effectively and locally as well as systematically.

**Preparation of lollipop:** It was designed to prepare candy based lollipop by heating and congealing method using specific polymer.

**Step-1:** The desired quantity of sugar was discovered in water by heating and stirring in a copper kettle until the sugar was completely dissolved. Corn syrup was added when the cooking temperature reaches 110°C. Cooking was then continuous to 145-156°C till the syrup base becomes thick.

**Step-2:** The finished cooked syrup (15.4°C) was then placed in vacuum chamber which was maintained at 274mm hg for about 30 minutes to remove the traces of water molecules and to give plasticity to the base prepared.

**Step-3:** The candy base was then transferred to a water-jacketed stainless steel cooling table of 214 ft. for the mixing operation. This is done manually. During the mixing cycle the temperature of candy base (154°F) was brought to 90°C to from a solidified mass. A hydrogenated vegetable oil-based lubricant was spread on the table surface to alleviate this condition. At this stage, the drug, polymers, citric acid and other excipients such as sweetening agents, flavoring agents were added manually and mixed thoroughly.

**Step-4:** Then this solidified mass was poured into the calibrated mold.

**Step-5:** Formation of the individual lollipop

**Step-6:** The product (lollipop) placed on the desecrater. Then the dried lollipop is then in another container and lubricated with oil so that prepared lollipops should not sick to each other.

**Step-7:** The prepared lollipops were packed in the aluminum foil. [8]
Table 2: Formulation of medicated lollipop [20]

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candy base</td>
<td></td>
</tr>
<tr>
<td>a. Sugar:</td>
<td>Dextrose, sucrose, maltose, lactose.</td>
</tr>
<tr>
<td>b. Sugar free vehicles:</td>
<td>Mannitol, sorbitol, polyethylene glycol (PEG) 600 and 800.</td>
</tr>
<tr>
<td>c. Fillers:</td>
<td>Di calcium phosphate, calcium sulfate, calcium carbonate, lactose, microcrystalline cellulose</td>
</tr>
<tr>
<td>Lubricants:</td>
<td>Magnesium stearate, calcium stearate, stearic acid and PEG, vegetable oils and fats.</td>
</tr>
<tr>
<td>Binders:</td>
<td>Acacia, corn syrup, sugar syrup, gelatin tragacanth and methylcellulose.</td>
</tr>
<tr>
<td>Coloring agents:</td>
<td>Water soluble and lakolene dyes, FD &amp; C colors, orange color paste, red color cubes, etc</td>
</tr>
<tr>
<td>Flavoring agent:</td>
<td>Eucalyptus oil, menthol, cherry flavor, spearmint etc.</td>
</tr>
<tr>
<td>Whipping agent:</td>
<td>Egg albumin, milk protein, xanthan gum, starch, gelatin, pectin, algin and carrageenan</td>
</tr>
<tr>
<td>Humectants:</td>
<td>Propylene glycol, glycerin, sorbitol.</td>
</tr>
</tbody>
</table>

Evaluation studies:

Evaluation of physical properties of medicated lollipops: The formulated lollipop is evaluated for the following parameters.

Thickness: The thickness and diameters of the formulated lollipop were measured by using Vernier caliper.

Weight variation: The formulated lollipop was tested for weight uniformity. 20 lollipops were collectively and individually for the combined weight, the average weight of lollipop was determined, each lollipop weight was then compared with average weight to determine whether it is within permissible limits or not.

\[
%\text{weight variation} = \frac{[\text{average weight} - \text{Individual weight}]}{[\text{Average weight}]} \times 100
\]

Hardness: the lollipops crushing strength, which is the force required to break the lollipop by compression in the diametric direction was measured in triplicate using Pfizer tablet hardness tester.

Friability: the Roche friability test apparatus was used to determined the friability of the lollipops. Pre-weighted lollipop was placed in the apparatus, which was subjected to 100 revolutions. Then the lollipop was reweighed. The percentage friability calculated was using formula. [19]

\[
%\text{friability} = \frac{[\text{Initial weight} - \text{Final weight}]}{100}
\]
**Drug content:** lollipop dissolved in 100 ml distilled water and sonicated 30 minutes and filtered from the above solution 1ml was taken in the volumetric flask and diluted up to 10 ml (100μg/ml) and it has analyzed by spectrophotometer against appropriate blank.

**Moisture content:** The sample was weighed and crushed in a mortar. From this, one gm of the samples was weighted and placed in desiccators for 24 hours. After 24 hours the sample is weight accurately. The moisture content is determined by the abstracting the final weight from initial weight of lollipops.

**Disintegration test:** disintegration study performed by disintegration apparatus. Put one lollipop into each tube suspend the assembly in the beaker containing pH 6.8 phosphate buffer and operate without the disc 30 min remove the assembly from the liquid. The lollipop pass.

**In vitro drug release:** In-vitro release studies were performed using USP apparatus II (paddle type). The dissolution test was performed by using 900 ml of phosphate buffer (pH 6.8) 37±0.5℃, at 50rpm. The samples (5ml) were collected at predetermined time several time interval and replaced with equal volume of fresh medium and analyzed using UV-visible Spectrophotometer. Drug concentration was calculated from a standard calibration of and expressed as cumulative % drug release.

**Anti microbial assay:** 100 mg of the polymer sample were separately aseptically mixed with 9ml of sterile normal saline and pH adjusted to 7.1ml of each dispersion was mixed 20ml of sterile lactose broth and placed separately in Petri dish. And the plates were incubated 37±1℃ for 24hr. After the incubation period, the samples were observed for the presence of microflora.

**Taste masking test:** first the stability studies 10 healthy volunteers would be given to taste standard quinine solution (120-160mcg/ml) by swirling the solution in buccal cavity for 30sec. and spitting out the solution volunteers would be asked to rank them an bitterness scale (rank 1-5) after 30min, these volunteers would be asked to evaluate the taste of drug lollipop in the same manner and compare on the same scale. [20]

**Stability study:** stability studies for the lollipop were carried out at 40℃ at 75%RH for a period of 90 day. For every 15 days the parameters like, drug content, weight variation, color, hardness and moisture content were determined. [21]

**Medicated lollipop available in the market for pediatric patient:** [22-25]

- Lil’ giggles kid’s: cough, cold & throat medicated lollipop
- Yumearth: organics vitamin c pop
- Yummy earth: organic vitamin c pop
- Chloraseptic lollipop: sore throth medicated lollipop
CONCLUSION

The chocolate formulation has not determined commercial acceptance for delivery of a pharmaceutically active agent of that difficulty in formulating chocolate composition which incorporate particular active agents, organoleptic characteristics of chocolate are great for masking obnoxious flavors associated with same active agents and imparting a smooth and creamy texture to composition of active agents. Thus chocolate delivery provides a suitable palatable source for delivery of medicaments through the oral route in pediatrics. Chocolate consumption improves brain function. Chocolate, as a maintain health; hence, chocolate as medi-food, which promotes its nutritional functions and its therapeutic abilities. Medicated lollipop is easy to prepared and harmless these will have additional advantages of patient compliance, convenience and comfortless for efficient treatment including low does. Immediate onset of action, reduce dosage regimen and economy. It is a formulation which is a more physically accepted particularly by the pediatric patients.

REFERENCES

23. Organics Sour Pops (https://in.iherb.com/pr/yumearth-Organics-Sour-Pops-Assorted-Flavors-14-Pops-3-oz-85-g/44903?Ccode=IN&currcode=INR&langcode=en-