Hatem A. Hejaz*, Ayat Kanan, Mahmood Al Mohtaseb and Ameer Ja'bari

Development and characterization of paracetamol medicated lollipops

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Abstract

Objectives: The oral route is the most common route of administration of drugs because of the low cost of therapy, ease of administration, patient compliance, and flexibility in formulation. Taking oral medicine is extremely odious to some patients, such as pediatric and geriatric patients. Paracetamol is one of the most used antipyretic and analgesic drugs, used in the management of fever and headache. Difficulty in swallowing (dysphagia) is common among pediatric and geriatric patients. Accordingly, there is a need for a solid form of medicine that is in a form easy to take and swallow, such as lollipops. The main objective of the present research study is to provide a solid form of medicine that is in a form that makes it pleasant to take and swallow by pediatric, geriatric, and bedridden patients, and avoid the dangers of being swallowed as do the other solid forms in those patients. However, lollipop is designed to improve patient compliance, acceptability, transportation, etc.

Methods: In the present research study, an attempt has been made to prepare sugar-based paracetamol medicated lollipops for pediatrics, geriatrics, and bedridden patients to overcome the administration problem. The paracetamol medicated lollipops were prepared using sucrose and corn syrup. All the formulations prepared were subjected to various physicochemical parameters like hardness, friability, weight variation, drug content, etc.

Results: The hardness of these lollipops ranges between 8 and 11 kg/cm³ with good physical characteristics like taste and color, they have good stability and moisture content below 1% and no variation in the IR spectrum.

Conclusions: Conventional dosage forms have some limitations that make it hard to use in pediatric and geriatric patients such as dysphagia, while medicated lollipops are

found to be favorable by them and also effective in delivering the drug with advantages like bypass of the first-pass metabolism and increasing drug contact time in the mouth which increases its bioavailability. Paracetamol medicated lollipops can provide an attractive alternative formulation in the treatment of fever and pain in pediatric and geriatric patients because they are easily swallowed.

Keywords: acetaminophen; geriatric; medicated lollipops; paracetamol; pediatric.

Introduction

Paracetamol (Acetaminophen) is a non-steroidal anti-inflammatory drug (NSAIDs) and is prescribed most frequently. Chemically it is 4-hydroxy acetanilide. It is one of the most commonly used 'over-the-counter' analgesics for headache, mild migraine, musculoskeletal pain, dysmenorrhea, etc. Paracetamol is generally safe for human use at the recommended dose. But overdoses of Paracetamol can cause potentially fatal liver damage and in rare individuals, a normal dose can do the same. The safety and efficacy of a pharmaceutical dosage form can be guaranteed when its quality is reliable. The efficacy of a pharmaceutical dosage form generally depends on their formulation properties, and manufacturing methods, hence it is likely that the quality of dosage form may vary [1].

The oral route of drug administration is the most commonly used route of drug administration because of low-cost therapy, ease of administration, patient compliance, and flexibility in formulation. However, pediatrics, geriatrics, and bedridden patients show inconvenience swallowing of conventional tablets or capsules due to difficulties in swallowing with lesser amounts of water with the medication, unable to tolerate the taste of many drugs when formulated as liquid dosage forms, resulting in poor patient compliance [2]. Many approaches and attempts were carried out to enhance patient compliance dosage forms and the pharmaceutical companies are focusing on the development of new drug delivery systems for the existing drug as the development cost of a new drug is very high [3]. Some of these approaches somehow improved patient compliance, but still, no dosage form

*Corresponding author: Dr. Hatem A. Hejaz, College of Pharmacy & Medical Sciences, Hebron University, P.O. Box 40, Hebron, Palestine, E-mail: hhejaz@hebron.edu

Ayat Kanan, Mahmood Al Mohtaseb and Ameer Ja'bari, College of Pharmacy & Medical Sciences, Hebron University, Hebron, Palestine

gives optimum compliance. However, there is a need for a solid form of medicine that is in a form that easy to take and swallow.

As mentioned, one of the major problems in pediatrics and geriatrics patients; they cannot take drugs in the conventional oral route, i.e., swallowing tablets, that's why drugs prepared in solutions or suspensions, but most of these formulated drugs have a bitter taste, even if they masked or prepared in sugary syrup. Another problem with these preparations, they will be absorbed through the intestine and undergoes metabolized (first-pass effect) in the liver. Thus, they will require more dosing frequency which is noncompliance in pediatrics patients since they resist taking medications [4]. These challenges need to develop new methods to overcome these challenges and produce a formula that will be effective and appealing to consumers as well that's when things like medicated candy lozenges and lollipops came to the surface and as it turns they had a lot of advantages especially lollipops.

Fever is a common complication that accompanies most diseases in humans, the body's natural response to any kind of inflammation wither it was viral, bacterial is an increase in body temperature. Pediatrics have a fever on regular basis because of their developing immune systems that most antigens are quite new for them and the body requires full inflammation cascade to produce proper antibodies. Since that very high body temperature can risk the child's health; physicians tend always to prescribe anti-pyretic drugs like paracetamol or ibuprofen to help the body fight against the disease while maintaining a low-risk temperature and to decrease the discomfort the patient is feeling. Besides, the high safety margin of paracetamol, and its common use in the treatment of fever among pediatric and geriatric patients required to develop a suitable dosage form of this drug which easy to take and swallow by them [5].

Medicated Lollipops are defined as hard dosage forms that contain one or more kind of a drug that is in a sugary base that is flavored and colored, these lollipops like any kind of lollipops are meant to dissolve slowly in the mouth of the patient and release its contents that might act locally to reduce oropharyngeal symptoms or to be absorbed through the buccal route and act systematically [6]. Medicated Lollipops can contain different kinds of drugs that can be antibiotics, antitussives, analgesics, and so, in the case of a drug like paracetamol, this type of formulation helps increasing its bioavailability and avoids the first-pass metabolism. Other advantages for this dosage form are increased patient compliance especially pediatrics, suitable to patients who trouble swallowing, it requires less time and cost in production, and decrease the dosing

frequency for the patient due to decreased drug waste in metabolism [7].

In light of all these challenges and the advantages of this dosage form, we were determined to develop and produce an effective, cost-efficient, and practical medicated lollipop that contains paracetamol as the prototype. Based on the results we are intended to develop such dosage forms with other commonly used drugs in pediatrics and geriatric patients to improve patient compliance and might be introducing this dosage form in the Palestine market as the Palestinian pharmaceutical market lacks such dosage form.

Materials and methods

Paracetamol was obtained from Sigma Aldrich, sucrose and dextrose were obtained from Firas library; corn syrup was obtained from a local store (commercial).

Phase-1 studies

Pre-formulation studies of paracetamol: Pre-formulation phase focuses on the concepts of physicochemical properties of the pure drug substance and when it is mixed with excipients. Pre-formulation studies are the first step in the rational development of a drug molecule to develop a safe, effective, and stable dosage form [7, 8].

Phosphate Buffer (pH 6.8) was prepared according to the procedure available online resource [9].

Confirmation tests of paracetamol were carried out including melting point, the solubility in different solvents, IR etc. The melting point of paracetamol was determined using the capillary method and found at 170 °C [10]. The solubility of the paracetamol was determined in different solvents as the following: A semi-quantitative determination of solubility was tested by adding approximately 10 mg of paracetamol to a fixed volume of solvents like phosphate buffer (pH 6.8), paracetamol found to be very slightly soluble in cold and hot water, and some organic solvents like ethanol, methanol, ethyl acetate, and acetone.

Determination of $\lambda_{\max}$: A UV absorption maximum was determined by appropriate dilution of standard stock solutions of paracetamol with phosphate buffer (pH 6.8) solution containing 10 µg/mL of paracetamol and was scanned separately between 200 and 400 nm (with 5 nm spectral bandwidth) using UV-visible spectrophotometer. The wavelength of absorption maxima was determined for the drug. Paracetamol showed absorption maxima at 243 $\lambda_{\max}$. A Standard stock solution of paracetamol (1,000 µg/mL) was prepared in phosphate buffer solution (pH 6.8) and from this; a solution (100 µg/mL of the drug) was prepared in phosphate buffer (pH 6.8) too. Thus, a series of diluted solutions of the drug with different concentrations were prepared and their absorbance was analyzed at 243 $\lambda_{\max}$ and a calibration curve was plotted between absorbance and concentration to get the linearity and regression equation. The IR spectrum of the drug and excipients was obtained in a KBR pellet using an FT-IR spectrophotometer. FT-IR spectra were recorded in the region of 400–4,000 cm^{-1} .

Assigning the major absorption bands changes indicates incompatibility between drug and excipients.

Phase-2 studies: preparation of medicated lollipops and basic physical tests

Preparation of syrup base: Syrup base was prepared by dissolving 66.66% w/v sucrose in purified water at 110 °C and continue stirring for about 30 min. Scaled downtime to appropriate with the quantity of material used was notice.

Preparation of medicated lollipops: Medicated lollipops of 5 g were prepared by heating and congealing technique. The base was prepared in a beaker dissolving sucrose in the water while heating and stirring at 110 °C for about 20 min, followed with corn syrup addition and stirring continued for 30 min, while raising the temperature to 160 °C. The material was left to cool, and the temperature was brought down 90 °C till a semi-plastic mass was obtained. Drug, polymer, coloring, and flavoring agents were added and mixed the materials for 10 min. After mixing all the ingredients the mixture was poured into silicone molds that had a diameter of 3 cm and 6 mm thickness, then it was wrapped with aluminum foil and left to solidify at room temperature. The details of the formulations are given in Table 1 [11, 12]. The ideal time of this step was determined by taking a small amount of the mixture using a glass rod and placed it in the beaker containing water would transfer to the solid-state directly at this moment the mixture was poured into silicone molds.

Evaluation studies

Evaluation of physical properties of medicated lollipops was evaluated for the following parameters:

Weight variation: Twenty lollipops were taken and their weight was measured individually then the whole amount was weighted, and the average weight was calculated. The individual weights are compared with the average weight. The sample complies with USP standard if no more than two lollipops are outside the percentage limit and if no lollipop differs by more than two times the percentage limit, this

criteria is similar to the tablets dosage form. The percent deviation of weight also was calculated using the following formula:

$$\% \text{Deviation} = \left[\frac{(\text{IndividualWeight} - \text{AverageWeight})}{(\text{AverageWeight})} \right] \times 100$$

Friability: The friability test apparatus was used to determine the friability of the lollipops. Twenty lollipops were weighted, and their weight was noted and placed in the apparatus. The lollipops were rotated at 25 rpm for 4 min meaning 100 rpm. The lollipops were reweighted and the friability percentage was calculated using the following formula:

$$\% \text{Friability} = \left[\frac{(\text{Initial Weight} - \text{Final Weight})}{(\text{Initial Weight})} \right] \times 100$$

Hardness and thickness test: From each batch produced four lollipops were taken and their hardness was tested using a tablet hardness device and the average was calculated. The thickness of the formulated lollipops was also measured by using Vernier calipers.

Phase-3 studies: characterization of prepared lollipops

The prepared formulations were subjected to drug content uniformity, dissolution, and stability tests by the following pharmaceutical standard methods:

Determination of drug content: The content uniformity was tested by crushing 20 lollipops, and an amount equivalent to 100 mg of paracetamol was weighed and taken into 100 mL volumetric flask and dissolved in 100 mL phosphate buffer that has a pH of 6.8 and left on a shaker overnight, then it was filtered. From that 1 mL of solution was withdrawn and taken in 100 mL volumetric flask and the volume was adjusted with phosphate buffer (pH 6.8) up to 100 mL. The absorbance was measured using a UV spectrophotometer at a wavelength of 243 nm; using phosphate buffer (pH 6.8) as a blank.

Dissolution studies: *In-vitro* dissolution studies were conducted using USP dissolution test apparatus type II, in a 250 mL of phosphate buffer

Table 1: Formulas of preparation of paracetamol lollipops.

No.	Ingredient	Formulations					
		F1	F2	F3	F4	F5	F6
1.	Sucrose	66.6 g	44.4 g	70 g	133.2 g	80 g	144 g
2.	Dextrose	—	22.2 g	—	—	—	—
3.	Corn syrup	27.7	25.7	25 g	55.1 g	14 g	44 g
4.	Paracetamol	5 g	5 g	5 g	10 g	5 g	10 g
5.	Citric acid	—	1 g	—	—	1 g	—
6.	Hydroxyl propyl methylcellulose	—	1 g	—	1 g	—	1 g
7.	Flavoring agent	0.67 g	0.67 g	—	0.67 g	—	0.67
8.	Coloring agent	0.03 g	0.03 g	0.03 g	0.03 g	—	0.03 g
9.	Purified H ₂ O	100 mL	100 mL	100 mL	200 mL	100 mL	200 mL
10.	Total weight	100 g	100 g	100 g	200 g	100 g	200 g

(pH 6.8) at $37 \pm 0.5^\circ\text{C}$ temperature, and the paddle speed was fixated at 100 rpm. Sampling was carried out every 5 min until 30 min and the samples were detected using a UV- spectrophotometer at 243 nm, take note that to maintain sink conditions equal volumes of the sample were replaced. The samples were filtered and the drug content of paracetamol in each sample was analyzed after suitable dilution by UV-spectrophotometer at 243 nm.

Moisture content: One lollipop from each formulation were weighed and crushed in a mortar. From this, 1 g of the sample was weighed and placed in desiccators for 24 h. After 24 h the sample is weighed. The moisture content is determined by abstracting the final weight from the initial weight of the sample of lollipops.

Stability studies: Four lollipops were taken from each batch and were subjected to different conditions; these included a variation of temperature and humidity. Stability studies were carried out at 30°C at 65% relative humidity for 45 days. The drug content and organoleptic tests (physical appearance) were conducted to show the effect of these conditions on the dosage form. The drug contents were determined by UV spectrophotometer at λ_{max} 243 nm [13].

Results

The physicochemical properties of paracetamol were determined as mentioned earlier, the melting point was ranged from 168 to 170°C . Paracetamol has good solubility in hot water and phosphate buffer along with organic solvents like ethanol. The standard solution prepared in water gave a good UV spectrum and based on the absorbance of different concentrations of this solution a calibration curve was constructed. The absorbance of solutions of pure paracetamol drug was analyzed by UV spectrophotometer at λ_{max} 243 nm and a calibration curve was plotted between absorbance and concentration to get the linearity and regression equation.

The lollipops prepared had a good physical appearance with a good distribution of color and good taste (self-taste test), the thickness of the lollipops ranged from 5–5.4 mm and all formulations showed uniform thickness. The prepared lollipops also have an acceptable hardness

and weight variation as shown in Table 2. The friability was under 1% for all batches, indicating good strength of lollipops. Hardness values of the formulation ranged from 8–11 kg/cm², which indicate good strength of lollipops. In the weight variation test for lollipops; their average weight was between 4.98 and 5.31 g and the percent deviation is about $\pm 5\%$ (Table 2). The average percent deviation of all lollipops was found to be within the limit and hence all formulation passes the weight variation test. Moisture content in the given lollipops ranged from 0.57 ± 0.03 to 0.42 ± 0.02 . The drug content was found to be uniform among all formulation and ranged from 94.85 ± 0.39 to $97.33 \pm 1.15\%$, all the data were shown in Table 2.

All the six formulations (F1–F6) prepared were subjected to an *in-vitro* release study. The *in-vitro* method to study the release rate should be so that it must simulate the mouth condition. In the present study, an *in-vitro* release study was carried out using a dissolution apparatus. For different time intervals, the sample was withdrawn and drug release was calculated. The dissolution apparatus USP II paddle-type was used. The temperature was maintained at $37 \pm 0.5^\circ\text{C}$ and stirred at 100 rpm. The dissolution medium used was phosphate buffer of pH 6.8. The samples were withdrawn at 5 min intervals for 30 min. The results of the drug release in the formulations are given in Table 3 and Figure 1 [14, 15].

Stability studies for the lollipops were carried out at 30°C at 65% relative humidity. After 45 days the physical appearance and the drug content were determined. The drug contents were determined by UV spectrophotometer at λ_{max} 243 nm. Table 4 shows the % age of drug contents of all the formulas before and after stability studies [15, 16].

The behavior of paracetamol after adding double distilled water was studied as described in Figure 2. It is seen from the spectra that in the case of the original paracetamol spectrum (A) the –OH and –NH stretching is dominant along with absorption by groups like amides. An increase in water addition (B) to (C) results in domination

Table 2: Physicochemical parameters of prepared paracetamol lollipops.

Parameter	Standard limits	F1	F2	F3	F4	F5	F6
Average weight		5.25 g	5.31 g	4.98 g	5.07 g	5.03 g	5.22 g
%Deviation	$>220 \text{ mg} \pm 5\%$	+2.3%	+3.5%	–2.9%	–1.16%	–1.19%	+2.2%
Thickness	$>12.5 \text{ mm} \pm 5\%$	5.10 mm	5.40 mm	5.20 mm	5.0 mm	5.25 mm	5.35 mm
Hardness	–	8	11	9	10	8	8
Friability		0.93 ± 0.01	0.96 ± 0.01	0.95 ± 0.01	0.95 ± 0.01	0.94 ± 0.01	0.92 ± 0.01
% Drug content		95.98 ± 1.09	96.06 ± 0.86	96.87 ± 0.11	97.33 ± 1.15	95.79 ± 1.36	94.85 ± 0.39
Moisture content		0.51 ± 0.04	0.53 ± 0.02	0.43 ± 0.11	0.42 ± 0.02	0.47 ± 0.06	0.57 ± 0.03

Table 3: *In-vitro* dissolution data of paracetamol medicated lollipops.

Time (min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	09.41 ± 1.25	10.01 ± 2.5	09.83 ± 1.43	09.77 ± 1.75	10.15 ± 1.01	09.63 ± 3.06
10	19.50 ± 4.60	20.03 ± 2.43	19.76 ± 1.78	20.11 ± 3.22	20.09 ± 1.56	19.85 ± 2.13
15	28.33 ± 1.87	30.91 ± 2.53	31.04 ± 4.26	31.5 ± 2.98	29.75 ± 1.70	30.61 ± 1.97
20	48.80 ± 1.67	50.74 ± 2.06	51.66 ± 2.32	50.89 ± 3.57	49.93 ± 1.09	48.67 ± 2.45
25	75.37 ± 1.44	74.90 ± 2.67	76.00 ± 2.89	76.30 ± 1.05	75.55 ± 1.24	75.62 ± 0.89
30	88.31 ± 0.72	88.48 ± 1.08	89.71 ± 0.66	89.67 ± 1.07	88.79 ± 2.04	89.13 ± 0.03

Figure 1: *In-vitro* drug release profile of different formulations.

of –OH stretching over –NH stretching due to the addition of more and more –OH ions from water to paracetamol along with diminishing of spectra from 1700 to 800 cm^{-1} region. The spectra obtained at a very low concentration of paracetamol in aqueous solutions are almost of the same shape as true for pure water. Similar FTIR studies for paracetamol in the water at room temperature have also been conducted by other researchers and they are identical with our results [16].

Discussion

Patient compliance is one of the important aspects of the administration of drugs. In the present study, paracetamol sweetened lollipops were designed for the effective treatment of pain and fever in pediatric and geriatric patients. Paracetamol or acetaminophen is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever

Figure 2: FTIR spectra of pure Paracetamol (A), aqueous Paracetamol (B), an aqueous solution of 5 $\mu\text{g ml}^{-1}$ Paracetamol (C).

reducer) by pediatric and geriatric patients. It is commonly used for the relief of headaches and other minor aches and pains and is a major ingredient in numerous cold and flu remedies. Difficulty in swallowing (dysphagia) is common among pediatric and geriatric patients. Accordingly, there is a need for a solid form of medicine that is in a form that easy to take and swallowed such as lollipops [17, 18].

In the development of a new dosage form, certain steps need to be considered before starting the preparation of the formula; especially to eliminate the interference of selected materials. These steps include purity testing, the melting point, and the basic analytical needs such as the UV calibration curve. The melting point of paracetamol as mentioned was measured by the capillary method and found in the ranged 168–170 $^{\circ}\text{C}$ thus; the material is of good quality and purity; these tests were confirmation tests.

Table 4: Drug content of different formulations before and after stability studies.

	F1	F2	F3	F4	F5	F6
Before stability study	95.98 ± 1.09	96.06 ± 0.86	96.87 ± 0.11	97.33 ± 1.15	95.79 ± 1.36	94.85 ± 0.39
After stability study	94.76 ± 0.55	95.38 ± 1.01	94.87 ± 1.31	95.74 ± 0.24	93.33 ± 1.04	92.21 ± 0.12

A standard solution of paracetamol was prepared by dissolving a calculated amount of the drug with phosphate buffer (pH 6.8) to construct the calibration curve that is used in the different testing and studies. The UV spectrum of paracetamol in phosphate buffer (pH 6.8) showed maximum absorption at λ 243 nm as mentioned. Hence the drug used in the formulation was found to be pure and the specifications were identical too. The UV spectrum of the paracetamol in phosphate buffer (pH 6.8) was performed.

Preparation of the lollipops was the hardest and time-consuming step in this research, the substances percentages, temperature, and time were crucial for the success of the formulation; as any slight change in any of these parameters and not abiding by the procedure and values as explained in the preparation section will lead to unsatisfactory results [7]. For example, temperature changes will produce lollipops that will start dissolving in the hands of the patient due to body temperature and this will affect the compliance and drug stability in the long run [19], and an increase in the time produces a very hard product; which will increase dissolution time and drug release, and as a result, this will be unpleasant to the patient. On the other hand, decreasing the time gives a semi-solid base that won't take the shape of the mold. Changing the percentages of sucrose to corn syrup, as in the formulas F5 and F6, does not mask the taste due to the decrease in the amount of corn syrup as noticed in F5 (no optimum masking the bitter taste), while F6 was too viscous this affected the dissolve of the drug, this means that the uniform distribution of the drug will be affected and some lollipops might have slight or no drug. In formula F2, the addition of dextrose had no observable effect. Thus, it is important not to change the different parameters of preparations as mentioned. Despite these, all the formulas contained optimum amounts of paracetamol. Citric acid was added to give a slightly sour taste to the formulas and to be consistent. The addition of the coloring and flavoring agent aims for a lime taste as reported. The hydroxypropyl methylcellulose was added as a surfactant and this will also increase the binding between the different materials in the formula. The formulas and preparation of lollipops including their numbers were designed to produce lollipops each contains 500 mg of paracetamol as a prototype; the recommended dose for adults but the future formula will contain 250 mg of Paracetamol; the recommended dose for children; age greater than two years old, with individualized dose frequency as either every 4 h or every 6 h depending on the patient condition and severity of the fever. The formula F4 gave the most satisfactory results, it had a good shape, and symmetrical distribution of color, and a sweet taste without any traces of paracetamol bitterness i.e., complete masking of

the taste. Lollipops of F4 formulation weighted 5.07 g in average and 5 mm thickness; all formulas had an acceptable friability of less than 1% and good hardness and minor weight deviation of about $\pm 5\%$ which is acceptable according to the International Council for Harmonisation (ICH) guidelines. A friability test was carried out to find how much the lollipops can withstand during their manufacturing, distribution, and handling by the customer. The strength of lollipops plays a very important role in its marketing and dissolution.

The lollipops prepared had a good physical appearance with a good distribution of color and good taste. All formulations showed uniform thickness. The prepared lollipops also have an acceptable hardness and weight variation as shown in Table 2. The friability for all batches indicates the good strength of lollipops. Hardness values indicate good strength of lollipop in all batches too. The percent deviation is acceptable according to the ICH guidelines. The samples comply with USP standard as no more than two tablets are outside the percentage limit ($\pm 5\%$ is the maximum % difference allowed) thus, lollipops pass the uniformity of weight/weight variation test. The average percent deviation of all lollipops was found to be within the limit ($\pm 5\%$) and hence all formulation passes the weight variation test as shown in Table 2. Moisture content in the given lollipops and the drug content were found to be uniform among all formulation and acceptable, as shown in Table 2. However, all lollipops were found to be within the limit and hence all formulation passes the different tests. There is no change in physicochemical properties after performing stability studies or slightly changed only in the drug contents as shown in Table 4. The drug content was found to be uniform among all formulations.

Dissolution is defined as mass transfer from the surface of the dosage form to the bulk of the solution. Dissolution is of primary importance for all conventional, solid, and oral dosage forms and can be the rated limiting step for the absorption of drugs administered orally especially for lipophilic drugs. Two objectives in the development of *in vitro* dissolution test are to show (i) release of drugs from the dosage form is as close as possible to 100% and (ii) that the rate of drug release is uniform batch to batch. Dissolution test is one of the *in vitro* tests usually employed to assess the quality of solid dosage forms such as tablets and capsules. During the dissolution test, the cumulative amount of drug that passes into the solution is measured as a function of time. The test thus describes the overall rate of all the processes involved in the release of the drug into the bioavailable form [20–23]. *In vitro* dissolution tests can be used to guide formulation development, identify critical manufacturing variables. Thus, the dissolution rate of the

lollipops prepared was studied using phosphate buffer (pH 6.8) for the remaining hours under sink conditions using USP dissolution apparatus type II. The theoretical release profile calculation is important to evaluate the formulation for release rates and to ascertain whether it releases the drug in a predetermined manner. Hence by the determination of the *in-vitro* release data, it can be concluded that the drug release was faster in all preparations. All the formulas (F1–F6) of paracetamol lollipops, exhibited the highest dissolution (%) in 30 min (88–89%, Table 3) along with comparatively highest drug content (95–97%, Table 4). The *in vitro* dissolution profiles were found to be varying for each formula but within the prescribed limit. According to the information found in the USP and BP show that paracetamol dissolves by 80% for 30 min. The dissolution of the medicated lollipops produced compliance of ICH 8 guidelines [24] and no shifting in the peaks of paracetamol in the FTIR spectrum; this means that there is no interaction between the drug and other excipients [7]. There is a slight exception in the case of dissolution profile is that the use of 100 rpm to simulate tongue movement effect while other studies used 25 rpm and a volume of 900 mL considering the lollipops the same as normal tablets. The color, taste, and appearance were determined, but proper standard tests required not individual tests as we have done. The stability testing was conducted by determining the drug content of all batches to measure the effect of different conditions and to make sure that the formulas stay stable for long periods. At the time of the first introduction of the product in the market, the stability samples of every batch may be taken, which may be decreased to only 2–5% of marketed batches at a later stage. Thus, the stability studies of all the formulas for lollipops (F1–F6) are only $\leq 2\%$ as shown in Table 4. Further stability studies should be carried out for different temperatures, relative humidities, and longer time, and the drug release should be calculated in interval times. However, different formulas (F1–F6) were designed with different excipients and drug contents as shown in Table 1, to study if the differences between these formulas affect the physicochemical parameters, dissolution, and *in vitro* release of the prepared paracetamol lollipops. Few differences were there and the formula F4 gave the most satisfactory results as mentioned previously.

In summary, this present research study is an attempt to formulate and evaluate medicated lollipops of paracetamol for the treatment of fever and pain in pediatric and geriatric patients to overcome the bitter taste and dysphagia among those patients. Medicated lollipops of paracetamol were prepared by the heating and congealing method. In this study, various formulations were

developed and evaluation parameters like thickness, weight variation, hardness show that they were within the limits. Drug content uniformity was also found to be within the limit. *In vitro* release rate studies showed that the drug release was acceptable. The possible interaction between the drug and excipient was studied by FT-IR spectroscopy which showed that there was no interaction between the paracetamol and selected additives. Thus, paracetamol medicated lollipops could be cost-effective and slow release in the oral cavity. Besides, it is a safe and effective dosage form for pediatrics and geriatrics patients and might have better bioavailability. The medicated lollipops can be prepared with other drugs especially the common one in pediatrics and geriatrics patients to overcome the administration problems. Further studies are needed to estimate how much of the drug is absorbed.

Conclusion

Medicated lollipops are one of the promising new dosage forms that if perfectly prepared and will have a great impact on the pharmaceutical market as it introduces a new and easy way of administering drugs to pediatrics. Such dosage forms are welcomed by both parents and children while still maintaining high effectiveness and bioavailability and most importantly, an increase in patient compliance. Besides, it is an easy, cost-effective, and time-saving process. In other words, medicated lollipops will be ideal dosage forms for pediatric patients as they have many additional advantages such as patient compliance, convenience, and comforts for efficient treatment including; low dose, immediate onset of action, reduced dosage regimen, and economical factor. These will offer a better innovative dosage form. Medicated lollipops will enjoy an important position in pharmacy and this will continue in the future.

Limitation of the study

Further investigations are required with optimum formula and large batch size; including stability studies, the drug release before and after stability studies, etc.

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