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FORMULATION AND EVALUATION OF CHOCOLATES CONTAINING GUAIFENESIN

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ABSTRACT

A part from the dosage form, organoleptic properties of the drug need to be given is a serious thought during the manufacturing process. Improved patient compliance can be obtained by delivering active pharmaceutical ingredient in an attractive form which results in reduced rejection / psychological inhibition towards dosage forms. The main objective the present investigation is to design and evaluate guaifenesin in the form of chocolate so as to improve patient compliance with ease of administration by all age group of patients. In the present study guaifenensin chocolates were prepared by heat method using cocoa butter, normal butter, cocoa powder, milk powder, icing sugar and sodium benzoate. Prepared chocolates were evaluated for physical appearance, hardness, stability, drug content, melting point and drug release studies. Best formulations of cocoa butter and normal butter were then compared with marketed formulation. Type of butter used in the preparation did not influence much in the drug release pattern from the chocolate form. Chocolates prepared using normal butter gave linear drug release similar to the marketed formulation when compared to the chocolates prepared using cocoa butter. All the formulations were stable for a period of month and concentration of sugar played a role in the taste of chocolate and its acceptance. Guaiphenesin chocolates with satisfactory results were successfully prepared using cocoa butter and normal butter by heating method. It was concluded that chocolates of various drugs with desirable drug release pattern can be prepared to increase patient compliance of different age groups.

KEYWORDS: Chocolate dosage form, Cocoa butter, Guaifenesin, Icing sugar, Organoleptic properties.

INTRODUCTION

Now a days, every prescription consists of various categories of drugs which need to be administered at regular intervals mostly by oral route this kind of frequent oral administration of various drugs make the patient uncomfortable due to difficulty in swallowing. Especially this is true in case of pediatric patients. By keeping this universal problem of pediatrics in mind most of the pharma companies coming out with various innovative formulations such as disintegrating tablets, dry syrups, lozenges, oral films etc. So that patients of any age can administer various drugs with much convenience improving patient compliance. A part from the dosage form, organoleptic properties of the drug need to be given is a serious thought during the manufacturing process. Improved patient compliance can be obtained by delivering active pharmaceutical ingredient in an attractive form which results in reduced rejection / psychological inhibition towards dosage forms. Keeping this in view a new attractive and highly acceptable form of formulation is developed.

Contrary to the common belief, it is not just children who are absolutely crazy about chocolate; several grown up men, women too just can seem to resist this sweet treat. Chocolate is highly sophisticated a versatile food that is combined to create completely different taste and texture sensations. Chocolate is also an anhydrous medium and is therefore resistant 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. For example, the organoleptic characteristics of chocolate are excellent for masking unpleasant flavours associated with some active agents and giving a smooth and creamy texture to composition of active agents that are otherwise undesirably gritty. Chocolate abundantly contains compounds such as saturated fats, polyphenols, sterols di and triterpines, aliphatic alcohols, and methyl xanthenes. Cocoa is the principle ingredient of chocolate and it is rich in polyphenols, particularly in flavin -3-ols such aqs epicatechins, catechins, and polycinides. Research studies suggest that a high intake of dietary flavonoids, a subgroup of polyphenols, chocolate may reduce the risk

of coronary heart disease. The antioxidant properties of flavanoids may partially account for the protective.

Effect.[1, 2] Anti tussives are most frequently accompanied by most of the other categories of drugs. guaifenisin is safe and frequently preferred antitussive by most of the present generation pediatrics. This made us to choose guaiphenesin for the present prestigious project. Guaiphenesin is an expectorant which increases respiratory tract fluid secretions and helps to loosen phlegm and bronchial secretions. By reducing the viscosity of secretions, guaifenesin increases the efficiency of the cough reflex and of ciliary action in removing accumulated secretions from the trachea and bronchi. Guaifenesin is readily absorbed from the gastrointestinal tract and is rapidly metabolized and excreted in the urine.[3] The present investigation is developed with an ultimate objective of developing a patient friendly guaiphenesin chocolate formulation using various combinations of sweetening agents and different types of butter.

MATERIALS AND METHODS

Materials

Guaiphenesin was obtained from Hetero drugs Pvt. Ltd, Hyderabad, cocoa butter and cocoa powder were obtained from Patiswarar natural greens and Girijan cooperative corporation Ltd., Vizag respectively. Milk powder and icing sugar were purchased from local market. All the other ingredients used in the study are of analytical grade.

Preparation of chocolates

For the formulation of each chocolate form drug, cocoa butter, cocoa powder, milk powder, icing sugar and sodium benzoate were used. All ingredients were weighed accurately. Required amount of cocoa butter and icing sugar was taken in porcelain disc. A glass beaker half filled with water was placed on tripod stand. Burner was set below tripod stand to heat water of beaker. On the top of beaker, a porcelain disc containing cocoa butter and icing sugar were placed. When water from the beaker was evaporated, due to the steam porcelain disc was heated and contents were melted. To this melt, a cocoa powder and milk powder were added and mixed. Finally specified amount of drug was added and mixed properly. These melted contents were poured to pre lubricated mould. Moulds were stored in a freeze for 45 min to solidify the contents.[4] This solidified content was removed from mould carefully and evaluated using various evaluation parameters. Formulation of the anti tussive chocolates was given in Table 1.

Table 1: Composition of Guaiphenesin chocolate formulations.

S.No	Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	Guaiphenesin (mg)	200	200	200	200	200	200	200	200
2	Cocoa powder (g)	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
3	Cocoa butter (g)	1.0	1.25	1.5	1.7	-	-	-	-
4	Normal butter (g)	-	-	-	-	1	1.25	1.5	1.7
5	Milk powder (g)	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
6	Icing sugar (g)	1.5	2.0	2.5	3	1.5	2.0	2.5	3
7	Sodium benzoate (g)	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
8	Total weight (g)	4.74	5.49	6.24	6.99	4.74	5.49	6.24	6.99

EVALUATION OF MEDICATED CHOCOLATES[2, 4-7]

Physical parameters

Shape and colour guaifenisin chocolate were evaluated by visual observation. Fragrance of guaifenesin chocolate was evaluated by smelling the guaifenisin chocolate and taste by volunteers. The dimension of chocolate such as diameetr and height for prepared chocolates was measured by vernier callipers.

Weight variation test

To study weight variation individual weights (W_I) of 20 chocolates from each formulation were noted using electronic balance. Their average weight (W_A) was calculated. Percent weight variation was calculated as follows. Average weights of the chocolates along with standard deviation values were calculated.

$$\%\text{weight variation} = \frac{W_A - W_I}{W_A} \times 100$$

Melting point of guaifensin chocolate

A glass beaker half filled with water was placed on tripod stand; burner was set below tripod stand to heat water of beaker. On the top of beaker, a porcelain disc containing guaifenisin chocolate was placed. A thermometer was placed in the porcelain disc. When water from the beaker was evaporated, due to the generated steam porcelain dish was heated and contents were melted. The melting temperature was measured using thermometer.

Hardness

Tablet hardness was measured by using Pfizer hardness tester. From each batch three tablets were measured for the hardness and average was taken.

Drug content of guaifenisin chocolates

Chocolates were crushed using knife and were dissolved in 100ml phosphate buffer solution by using magnetic stirrer for 15 min. This solution was then poured in centrifuge tube and then tube was put in centrifuge for 15

min at 3000 rpm. Centrifugation left two layers Upper layer with clear supernatant liquid containing dissolve drug and a lower chocolate base. The upper layer was then filtered to remove any traces of chocolate remaining in it. This liquid.

Physical observation

This study was performed to determine any interaction or physical changes that may occur when kept with various excepient at different environmental conditions. Drug was mixed with various excepient in the ratio of 1:5 and was kept in closed vials. These vials were placed at 25 ºC for 1 month. The vials kept at 28 ºC were considered to be control samples. After one-month interval, sample vials were withdrawn from each test group and physical appearance and drug degradation was observed.

***In vitro* drug release/dissolution studies**

The *in vitro* drug release studies were carried out on a eight stationed USP type II dissolution apparatus (paddle method) at 37 °C ± 0.5 °C and 50 rpm for a period of 1h. The dissolution studies were carried in triplicate in 900 ml of the phosphate buffer pH 6.8 from 45 min to 1 hr. An aliquot (5 ml) was withdrawn at specific time intervals and replaced with the same volume of pre warmed (37 °C ± 0.5 °C) fresh dissolution medium. The samples withdrawn were filtered through Whatsmann filter paper (No.1) and drug content in each sample was analyzed by UV-visible spectrophotometer at274 nm. The amount of drug present in the sample was calculated with the help of appropriate calibration curve constructed from reference standards.

RESULT AND DISCUSSION

For each designed formulation, blend of drug and excepient was prepared according to the formulae given in Table 1. Prepared chocolates were evaluated for shape, texture, colour, taste and dimensions. Results were given in Table 2. All the medicated chocolates are round in shape with specified dimensions. The texture of all the chocolates was creamy, smooth, not waxy and evenly melts in the mouth. All the formulations had pleasant and fresh chocolaty aroma.

All the medicated chocolates are round in shape with specified dimensions. The texture of all the chocolates was creamy, smooth, not waxy and evenly melts in the mouth. All the formulations had pleasant and fresh chocolaty aroma.

Table 2: General appearance and dimensions of chocolates (mean±S.D; n=3)

S.No	Formulation code	Appearance	Colour	Taste	Dimensions (diameter X height) cm
1	F_1	Glossy, even shine, no streaks	Dark brown	Slightly bitter	2.8X0.5±0.001
2	F_2	Glossy, even shine, no streaks	Dark brown	Neither bitter nor sweet	2.8X0.5±0.001
3	F_3	Glossy, even shine, no streaks	Dark brown	Semi Sweet	2.8X0.5±0.001
4	F_4	Glossy, even shine, no streaks	Dark brown	Sweet, good after taste	2.8X0.5±0.001
5	F_5	Not shiny, no streaks	Light brown	Slightly bitter	2.8X0.5±0.001
6	F_6	Not shiny, no streaks	Light brown	Neither bitter nor sweet	2.8X0.5±0.001
7	F_7	Not shiny, no streaks	Light brown	Semi Sweet	2.8X0.5±0.001
8	F_8	Not shiny, no streaks	Light brown	Sweet, good after taste	2.8X0.5±0.001

Formulated chocolates were evaluated for Physical characteristics such as hardness, melting, weight variation and drug content and the results were given in table 3. The hardness of the chocolates ranged from 2.1-3.1 kg/cm^2 and the melting point of the chocolates was between 34 – 36 ˚C. The drug content was found to be in acceptable range for all the formulations and weight of the chocolate was between 3.8 – 6.5 g.

Table 3: Physical characteristics of the medicated chocolates (mean±S.D; n=3)

S.No	Formulation code	Hardness (Kg/cm^2)	Melting point	Weight variation	Drug content (%)
1	F_1	2.1±0.01	34˚C	4.0±0.001	98.05±0.58
2	F_2	2.4±0.01	36˚C	5.0±0.001	99.8±1.33
3	F_3	2.3±0.02	34˚C	6.0±0.001	97.4±0.68
4	F_4	3.1±0.03	35˚C	6.5±0.001	99.5±0.78
5	F_5	2.3±0.01	34˚C	3.8±0.001	98.8±0.91
6	F_6	2.2±0.02	36˚C	4.9±0.001	99.1±0.89
7	F_7	2.5±0.01	35˚C	6.0±0.001	99.78±0.75
8	F_8	2.4±0.10	34˚C	6.4±0.001	98.79±0.82

Medicated chocolates were tested for their Physical stability and the results were tabulated in Table 4. The mixture of the ingredients found to be stable and the formulations are stable for a period of 1 month even stored at normal room temperature without any change in the physical characteristics.

Table 4: Physical observation of the medicated chocolates.

S.No	Storage condition for 1 month	General appearance
1.	2-8 ºC (Controlled)	No change
2.	25ºC/75% RH	No change

Chocolates containg drug were evaluated for *in vitro* drug release studies and the results were given in table 5. The dissolution data of the medicate chocolates was given in the Table 5 and 6. Figure 1, 2, 3 depicts the release profile of Guaiphenesin from the chocolates of containing cocoa butter, normal butter and comparative release of the optimized formulations with marketed tablets respectively.

Table 5: *In vitro* percent drug release data of Guaiphenesin from chocolates containing cocoa butter.

Time(min)	F_1	F_2	F_3	F_4
5	12.82±0.08	10.12±0.13	11.92±0.24	12.15±0.34
10	29.02±0.12	24.52±0.34	25.87±0.21	27.54±0.51
20	43.47±0.45	38.02±0.42	43.24±0.14	38.56±0.53
30	60.75±0.26	68.85±0.21	63.9±0.24	66.6±0.42
40	73.8±0.17	76.05±0.12	72.45±0.42	79.2±0.12
50	86.4±0.14	86.85±0.34	87.3±0.21	88.2±0.13
60	98.45±0.26	98.56±0.16	98.12±0.13	99.9±0.21

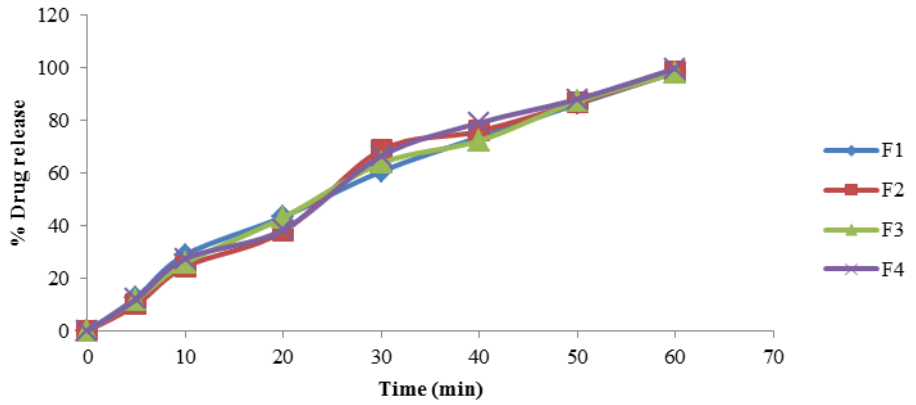

Fig.1: *In vitro* drug release profile of chocolates using cocoa butter.

Release profile of formulations containing cocoa butter indicated that there is no drastic change or noticeable change in the release of the drug and all most all the formulations released drug in a similar manner.

Table 6: *In vitro* percent drug release data of Guaiphenesin from chocolates containing normal butter

S.No	Time(min)	F_5	F_6	F_7	F_8
1	5	11.02±0.23	23.62±0.31	11.20±0.08	11.34±0.14
2	10	26.19±0.31	28.17±0.23	25.29±0.24	23.67±0.15
3	20	41.53±0.12	33.93±0.21	42.93±0.31	38.54±0.24
4	30	62.55±0.14	68.4±0.08	62.55±0.08	56.55±0.25
5	40	77.4±0.08	82.8±0.24	75.15±0.23	75.6±0.34
6	50	87.75±0.34	86.85±0.41	87.75±0.13	85.95±0.08
7	60	98.9±0.14	98.23±0.53	98.35±0.32	99.7±0.14

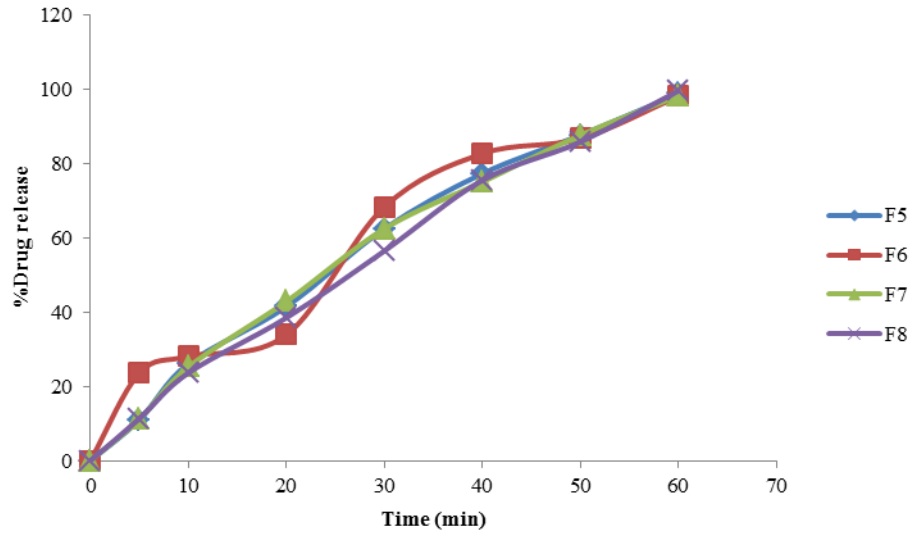

Fig.2: *In vitro* drug release profile of chocolates using normal butter

Release profile of formulations containing normal butter indicated that similar release of the drug where as F_6 has shown less uniform drug release pattern.

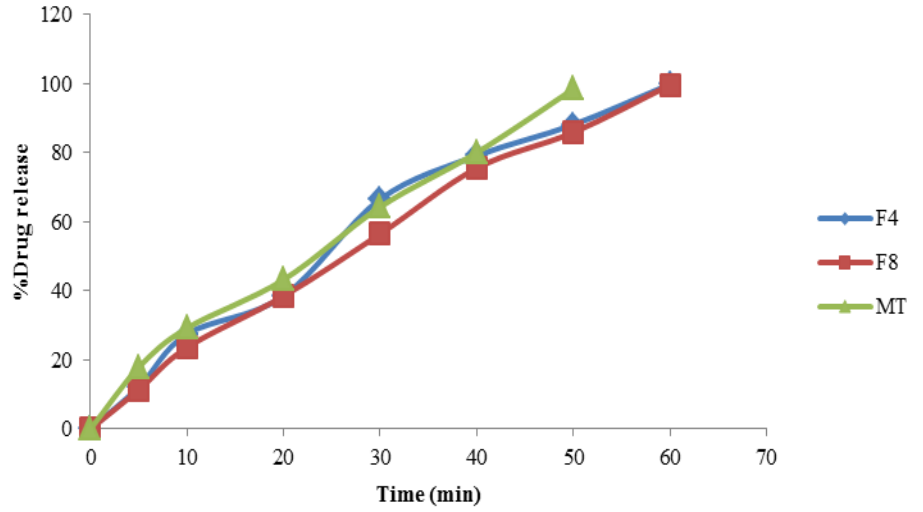

Fig.3: Comparative *In vitro* drug release profile of best formulations with marketed formulation.

In the above formulations F_4, F_8 containing cocoa butter and normal butter released 99% of drug where as marketed formulation released 98% drug. F_8 formulation has shown linear drug release similar to the marketed tablets though the drug released is slow and less. Whereas F_4 formulation did not show a linear drug release as that of F_8. Hence, the chocolates prepared using normal butter is considered as optimized formula for preparing guaifenisin chocolate dosage forms.

CONCLUSION

Guaiphenesin chocolates with satisfactory results were successfully prepared using cocoa butter and normal butter by heating method. Study indicated that both the butters used in the formulation had similar drug release pattern where as chocolates with normal butter released drug linearly when compared to the cocoa butter chocolates. All the formulations were stable for a period of month and concentration of sugar played a role in the taste of chocolate and its acceptance. It was concluded that chocolates of various drugs with desirable drug release pattern can be prepared to increase patient compliance of different age groups.

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REFERENCES

1. Buck ML. Alternative forms of oral drug delivery for pediatric patients. Pediatric pharmacotherapy, 2013; 19(3): 1–4.
2. Nidhi P, Saleha D, Kajal S, Priyanka T, Hitesh J, Prasanna P, Umesh U. Chocolate drug delivery system: a review. Indo American Journal of Pharmaceutical Sciences, 2015; 2(6): 1077-1081.
3. Sweetman SC. Martindale: The Complete Drug Reference. 24th ed. Great Britain. The pharmaceutical press, 2005; 2032.
4. Chirag V, Ketan S. Preparation and evaluation of chocolate drug delivery system of albendazole. Research journal of pharmacy and technology, 2016; 9(11): 1994-1998.
5. Sharma M, Dinesh Kumar J. Chocolate formulation as drug delivery system for pediatrics. Indonesian J. Pharm, 2012; 23(4): 216–224.
6. Janki Patel, Maulin J, Vaishali T, Mukesh G, Lalji B, Asha P. Medicated chocolate containing cefpodoxime proxetil: a novel solid dosage form for paediatric patient. RK University's First International Conference on Research & Entrepreneurship, 2016.
7. Majumdar SH, Bhongale AS, Aloorkar NH, Kulkarni AS. Development and Evaluation of a Chocolate Based Dosage Form Containing Shankha Bhasma. American Journal of Pharmacy & Health Research, 2016; 4(12): 32-47.