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DEVELOPMENT AND EVALUATION OF ONDANSETRON MEDICATED JELLY

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ABSTRACT

Aim of this study is to develop medicated jelly of Ondansetron for effective delivery in paediatric patient. It is the prototype of a new class of antiemetic drugs developed to control cancer chemotherapy/radiotherapy induced vomiting, and later found to be highly effective in postoperative nausea and vomiting as well. It blocks the depolarizing action of 5-HT through 5-HT3 receptors on vagal afferents in the G.I.T. as well as in NTS and CTZ. It is convenient to administer as compared with liquid dosage form in pediatric. This formulation is very good alternative for drug delivery to paediatrics, geriatric and dysphagic patients. Oral jellies have significant advantages of both solid and liquid dosage forms, as they remain solid during storage which aid in stability of dosage forms and transform in liquid like form within few seconds to minute after its administration. Medicated jelly is prepared by gelling agent like Gelatin and carbopol 934, other excipients and using sugar syrup. In-vitro dissolution were applied to interpret the release of Ondansetron. The F3 formulation was best and optimized formulation on the basis of dissolution profile and because of gelatin as jelling agent it was non sticky as compaired with carbopol 934 so that weight variation not occurred and having better dissolution.

KEYWORDS: Ondansetron, Gelatin, Carbopol 934.

1. INTRODUCTION

Oral medicated jellies have potential advantages over other conventional dosage form, with improved patient compliance, convenience and rapid onset of action. This kind of formulation is very good alternative for drug delivery to paediatrics, geriatric and dysphagic

patients. Oral jellies have significant advantages of both solid and liquid dosage forms, as they remain solid during storage which aid in stability of dosage forms and transform in liquid like form within few seconds to minute after its administration. Thus, oral jellies have tremendous scope for being the delivery system for most of the drugs in near future.

The benefits of these prepared jellies are increased bioavailability by-passing first pass metabolism. jellies were prepared by dispersing the gelling agent in water. Many therapeutic agents are absorbed in the oral cavity. For the drugs having significant buccal absorption, dosage forms such as Medicated Jelly and Chewing Gums permit more rapid therapeutic action as compared to oral dosage forms. Medicated Jelly has been very well received by the parents for their use in children with full dentition. The use of Medicated Jelly is feasible in local treatment of diseases of oral cavity as well as treatment of systemic conditions. They may be prepared form natural gums, such as tragacanth, pectin, sodium alginates or from synthetic derivatives of natural substance such as methyl cellulose and sodium carboxymethyl cellulose.

Ondansetron is the prototype of a new class of antiemetic drugs developed to control cancer chemotherapy/radiotherapy induced vomiting, and later found to be highly effective in postoperative nausea and vomiting as well. It blocks the depolarizing action of 5-HT through 5-HT3 receptors on vagal afferents in the g.i.t. as well as in NTS and CTZ.

Children may consider jelly as more preferred method of drug administration compared with oral liquid or tablets. The use of medicated jelly is feasible as local treatment of disease of the oral cavity as well as treatment of systemic condition.[1,2]

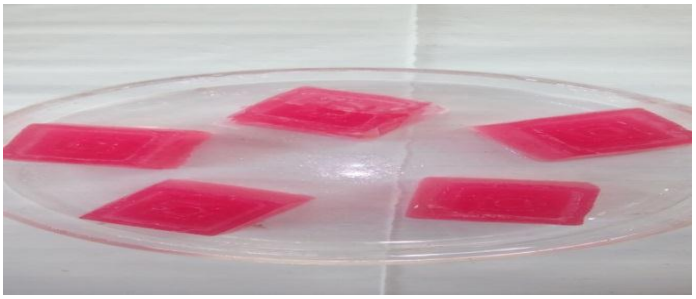

Fig. 1 Medicated jelly.

Advantages

1. It is convenient to administer – anywhere, anytime, doesn't require water.
2. The treatment can, if required, be terminated at any time.

3. It may prove to be particularly suitable for the systemic delivery of drugs, which are susceptible to metabolism in the gut wall or liver.
4. In addition, the drugs that are released from jelly and swallowed, will be introduced in the gastrointestinal tract either dissolved or suspended in saliva and thus will be present in a readily bioavailability form.
5. As a delivery systemic administration of drug via the oral mucosa it has the potential to overcome the problems of short lived action and variations in drug release and retention times.[3]

Disadvantages

1. Since it is aqueous preparation it requires proper packaging for safety and stabilization of drugs.
2. If not formulated properly, it may leave unpleasant taste in mouth.
3. Various stability problems occure due to synersis which separate water from the gel.[3]

2. MATERIALS AND METHODS

2.1. Reagents and Chemicals

Standard drugs of Ondansetron were kindly supplied as a gift sample by Alkem Lab. Lim. Parel, Mumbai. All the matrials used in the study are Gelatin, Carbapol 934, Dextrose, Citric acid, Methyl paraben, Sucrose were purchased from Merck Specialities Pvt. Lim, Warali Mumbai, Loba Chem. Pvt. Lim, Tarapur MIDC Boisar, Mumbai, Modern Industries C-74, Nashik, Thomas beaker chemical pvt lim. Marin drive Mumbai, Research lab fine chem. Industries Mumbai, Modern Industries C-74, Nashik.

2.2. Instrumentation

The various apparatus used were like

Electronic Balance CY 120(Citizen, Mumbai), Electronic Hot Air Oven 12(B) (Shital Scientific Industries, Mumbai), Magnetic Stirrer with Hot Plate(Omega Scientific Industry, Haryana), Dissolution Tester (USP) TDT-08L(Electrolab, Mumbai), UV-visible Spectrophotometer Carry 60(Agilent Technology, US), Stability Test Chamber LSC 170 G(Skylab Instruments & Eng. Pvt. Ltd., Thane).

2.3. Formulation of Ondansetron Medicated Jelly

Table 1: Formulation table for Ondansetron Medicated Jelly.

Sr. No.	Ingredients	F1	F2	F3	F4	F5	F6
1.	Drug(Ondansetron)	40 mg	40 mg	40 mg	40 mg	40 mg	40 mg
2.	Gelatin	3.5 gm	4gm	4.5gm	-	-	-
3.	Carbapol 934	-	-	-	3.5gm	4gm	4.5gm
4.	Dextrose	1 gm	1 gm	1 gm	1 gm	1 gm	1 gm
5.	Citric acid	0.5gm	0.5gm	0.5gm	0.5gm	0.5gm	0.5gm
6.	Methyl paraben	0.10gm	0.10gm	0.10gm	0.10gm	0.10gm	0.10gm
7.	Sucrose	33.4gm	33.4gm	33.4gm	33.4gm	33.4gm	33.4gm
8.	Colour	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.
9.	Flavour	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.
10.	Purified water	11.46ml	10.96ml	10.46ml	11.46ml	10.96ml	10.46ml

2.4.1 Preparation of Sugar Syrup

According to I.P. 2007, sugar syrup of 33.4% w/w was prepared as: Accurately weighed 33.4 gm of sucrose on digital electronic balance and it was transferred to 250 ml of beaker. To it 16.6 gm of water was added slowly with stirring continuously, and then kept for heating on heating mantle in order to get the supersaturated solution of sugar syrup.

2.4.2 Preparation Method of Jelly

1.All the ingredients will be weighed accurately.

2.In one beaker sugar syrup will be prepared by adding 67.7 gm of sugar in beaker and make up the volume up to 100ml.

3.To that solution gelling agent will be add with constant stirring and heated to dissolve to achieve desired stiffness.

4.When gelling agent will completely dissolve, stabilizer and citric acid will be added and again stirred to enhance softness of the jelly and to maintain pH respectively, and then boil for few minutes.

5.After boiling the above solution, preservative will be added to that solution, mixed thoroughly and uniformly.

6.Now drug is weight accurately, dissolved in suitable vehicle and added before jelly is allowed to set, mix thoroughly.

7.Then whole solution was transferred in to moulds and then allowed it for cooling and settling undisturbed by proper covering the moulds to avoid exposure to outer environment.

3 RESULT AND DISCUSSION

3.1 IR Spectroscopy

3.1.1 FTIR study of Ondansetron

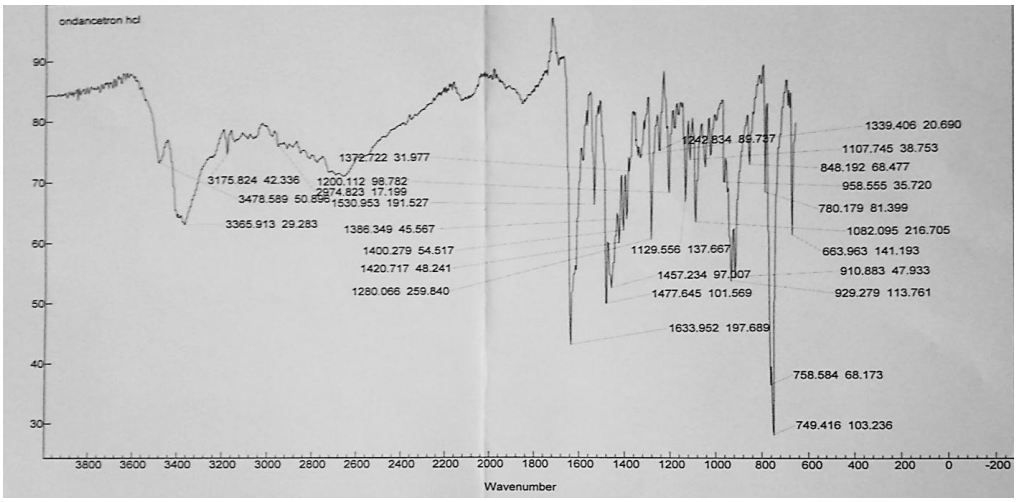

Fig. 2: IR spectra of ondansetron.

3.1.2 IR spectra of Drug+Gelatin+Carbapol 934

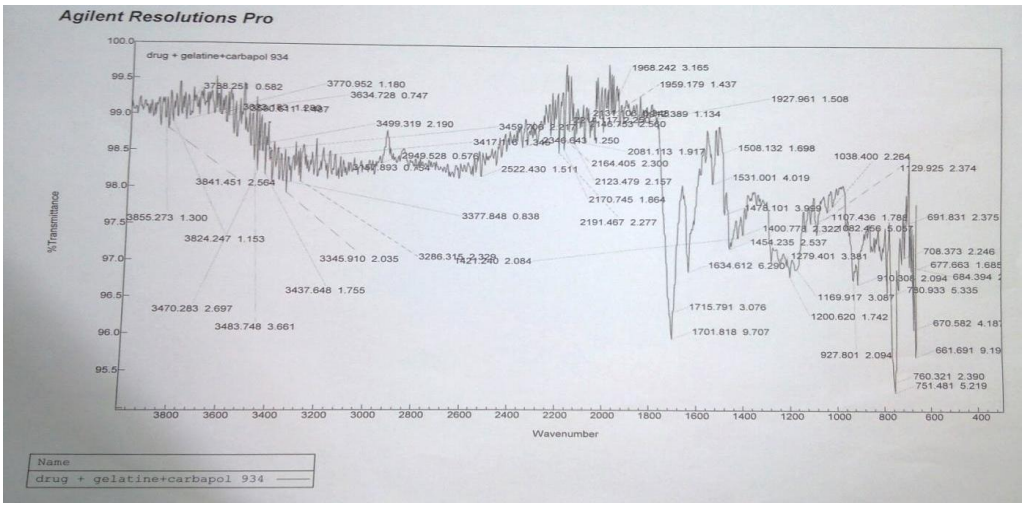

Fig. 3: IR spectra of Drug+Gelatin+Carbapol 934.

3.2 Physical parameter of jelly

Table 2: Physical parameter of Medicated Jelly.

Formulation	Solubility	Clarity	Consistency	Hand feel	Setting time
F1	Rapid	Clear	Not stiff	Non sticky	60 Min.
F2	Rapid	Clear Transparent	Not stiff	Non sticky	60 Min.
F3	Rapid	Clear Transparent	Not stiff	Non sticky	50 Min.
F4	Rapid	Clear	Little Stiff	Little sticky	30 Min.
F5	Rapid	Clear	Stiff	Little sticky	30 Min.
F6	Rapid	Clear	Stiff	sticky	20 Min.

From above observation, it was seen that batch-3 (F3) which was given desired properties.

3.3 In- vitro drug release: Dissolution test apparatus was used by taking 100 ml of pH 6.8 buffer in 100 ml dissolution flask and jelly was placed in it, rotating paddle at a speed of 50 rpm and temperature 37±1ºC was maintained. 1 ml aliquots were withdrawn at 05, 10, 15, 20, 25 and 30 minutes intervals, after each withdrawal of a sample an equal volume of dissolution medium was added to the dissolution flask. The filtered samples were diluted and analyzed spectrophotometrically at 248.0 nm.

Table 3: In-vitro dissolution data of F1 –F6 formulation.

Time	Cumulative Percent drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	9.25	33.12	24.25	19.5	51.75	23
10	12.5	43.75	41.5	40.75	69.25	44.25
15	56.5	45.75	55.75	56.5	90.5	64.25
20	45.25	66.75	62.25	81.5	102.25	95.75
25	56.5	69.75	70	110.5	108.75	141.5
30	65	72.75	81.25	122.75	113	163.75

The results of in vitro release of ondansetron from all formulations are shown in Figure 4,5.

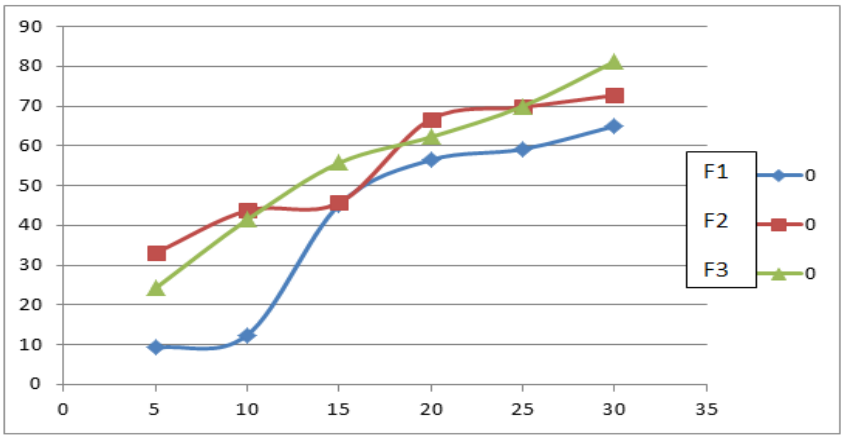

Fig. 4: In-vitro dissolution profile of F1– F3 formulation.

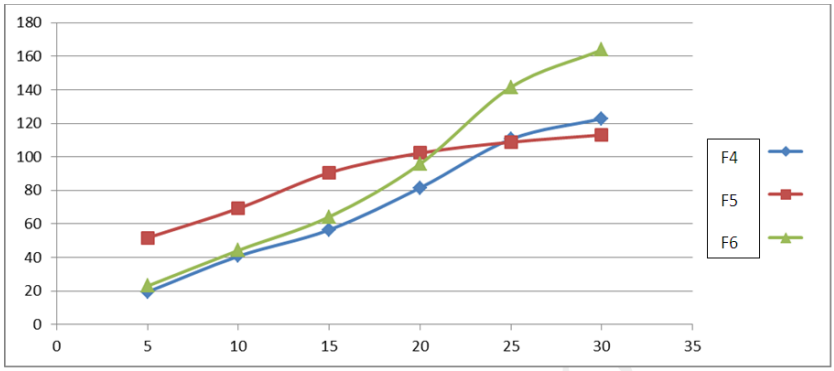

Fig. 5: In-vitro dissolution profile of F4– F6 formulation.

In-vitro release studies of all the formulations were also compared and evaluate. The results showed that the drug release profile of formulation F3 was considered as optimized formulation and used for further study.

3.4 Evaluation of optimized batch (F3)

3.4.1 Weight variation

The average weight of ten jellies was taken to determine weight variation. The jellies were taken out of the moulds in a beaker and weighed individually, pooled and mixed. The weight variation was found between **4.91%** in all prepared jelly formulations (F3).

Weight of 10 jellies	49.19 gm
Average weight of per jelly	4.91 gm

3.4.2 Determination of pH

The results of pH of prepared jelly formulations are summarized in Table 3. The pH of the formulation influences the taste and stability of oral jellies. The pH of the prepared formulations was found in the range of **4.10 ± 0.03** which was acidic. Sucrose may precipitate in the presence of citric acid on standing. Therefore, a minimum quantity of citric acid was added just to maintain the pH.

3.4.3 Content uniformity

The drug content of prepared Ondansetron medicated jelly of batches F3 was evaluated by using UV spectroscopy method. The drug content of F3 formulation was found to be in the range of **87.67%** which shows formulation have uniformity of content.

3.4.4 Syneresis

Syneresis was more pronounced in the formulations, where separation of water from gelling agent was employed. It was observed after **60 days** of jelly preparation. The formulations F3 showed syneresis at room temperature (25°C ± 5°C).

3.4.5 Stability studies

A physically stable medicated oral jelly should retain its viscosity, colour, clarity, taste, and odour throughout its shelf life. The samples were characterized for change in various parameters such as made sample was used for subjective evaluations. Formulation F3 showed best results. appearance, pH, viscosity, sugar crystallization, stiffness, syneresis and drug content at the end of 90 days.

Results of stability studies on optimized formulations after 30 days

Formulation	Temperature (°C)	pH	Drug content (%w/w)
F3	25°C	4.10	86.40

Results of stability studies on optimized formulations after 60 days

Formulation	Temperature (°C)	pH	Drug content (%w/w)
F3	25°C	4.05	84.05

4. SUMMARY AND CONCLUSION

Summary

In the market, no such formulation is tried as semisolid moulded gelatin or carbapol jelly containing any medicament. Especially as an antiemetic treatment, mostly syrup tablet are the dosage forms available. Considering disadvantages of marketed preparations and advantages gelatin or carbapol jelly as dosage forms, an attempt was made to formulate gelatin or carbapol jelly in such a way that it will be suitable for incorporation of medicament for the treatment of paediatric patient.

It is found that sucrose based Medicated jellies will be ideal dosage forms for patients. These will have additional advantages of patient compliance, convenience and comfortness for efficient treatment including low dose, immediate onset of action, reduced dosage regimen and economic. The Physico-chemical characterization revealed that all the formulations were found to be shown acceptable weight variation, pH, viscosity, spreadability and syneresis. The drug content estimation showed uniform drug content in all the formulations.

IR spectroscopic studies indicated that there were no drug-excipients interactions. polymers gelatn and carbapol yield good results to prolong dissolution time and the drug release in salivary pH conditions for a period of 30 minutes. The stability studies proved that the prepared Medicated jellies were found to be stable when stored at 25^0c. that zone inhibition of various prepared formulations was found to be equal on comparison with the activity of pure drug. This indicates that there is no change in the molecular activity of the drug present in the formulations.

Oral medicated jellies have potential advantages over other conventional dosage form, with improved patient compliance, convenience and rapid onset of action. This kind of formulation is very good alternative for drug delivery to paediatrics, geriatric and dysphagic

patients. Oral jellies have significant advantages of both solid and liquid dosage forms, as they remain solid during storage which aid in stability of dosage forms and transform in liquid like form within few seconds to minute after its administration. Thus, oral jellies have tremendous scope for being the delivery system for most of the drugs in near future.

The benefits of these prepared jellies are increased bioavailability by-passing first pass metabolism. jellies were prepared by dispersing the gelling agent in water. Many therapeutic agents are absorbed in the oral cavity. For the drugs having significant buccal absorption, dosage forms such as Medicated Jelly and Chewing Gums permit more rapid therapeutic action as compared to oral dosage forms. Medicated Jelly has been very well received by the parents for their use in children with full dentition. The use of Medicated Jelly is feasible in local treatment of diseases of oral cavity as well as treatment of systemic conditions.

CONCLUSION

In the present study, the jellies loaded with ondansetron were successfully formulated using gelatin, carbapol. The optimized formulations showed acceptable physico‑chemical properties and stability. Formulations **F3**, could be effectively employed for oral delivery for paediatric, geriatric and dysphagic patients as alternatives to solid oral dosage forms.

The study reveals that ondansetron oral jelly released the drug as rapid manner with improved bioavailability. The observed results were found that the concentration of gelatin carbopol 934 can influenced the release rate & other physico chemical properties. Thus it can be concluded that ondansetron jellies are beneficial in improving the bioavailability of drug as compared to other oral fast releasing dosage forms.

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