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FORMULATION AND EVALUATION OF DOMPERIDONE ORAL JELLY

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ABSTRACT

Oral medicated jelly is a novel oral dosage form. There is need to develop such dosage form in order to overcome difficulties faced by paediatric and geriatric patients in administration of conventional dosage form. It is highly beneficial for individuals with swallowing difficulties. Oral jelly can be chewed effortlessly & dissolves easily in saliva without any need of water for ingestion making it unique from other dosage forms. Further patients get fascinated by its appearance & soft texture resulting in high patient acceptance. In the present research work Domperidone jelly was formulated to provide faster relief from nausea & vomiting compared to other dosage forms. Jelly formulation is prepared using sucrose, gelatine, citric acid, sodium citrate, sodium benzoate by heating & congealing method. It is evaluated for appearance, weight variation, pH, synergesis, drug content, & dissolution. Optimized formulation has shown drug release of 98.39% in 25minutes.Medicated jelly (F5) has shown effective drug release compared to the soft chew formulation (F9). The stability studies on optimized formulation (F5) was carried out as per ICH guidelines & has shown acceptable result.

KEY WORDS

Medicated jelly, Domperidone, Nausea & vomiting, Heating & congealing, Nutraceutical

1. INTRODUCTION

In recent times, efforts are made for the development of novel drug delivery system as it offers supplementary benefits. Oral route is highly preferred for its diverse advantages; one amongst them is easiness in administration of medicaments. At present, the use of medicated jelly for delivering active pharmaceutical ingredients is gaining acceptance & it can also be used to meet the nutrition supplement in the form nutraceutical. In the world market, US is the forerunner with a share 20% in medicated jelly formulations.[1]

According to the Japanese Pharmacopeia (JP XVII), jellies are defined as non-flowable gelatinous preparations having a certain shape and size, meant for oral administration.[2]

Medicated jellies offers many advantages over conventional dosage forms: it can be masticated easily by elders & children because of its soft & smooth nature; children's mostly accept jelly dosage form compared to tablets due to its elegant appearance; it aids in treatment of xerostomia by stimulating flow of saliva; it can also be used for treatment of systemic disease & oral infections;[3] medicated jelly can provide rapid buccal absorption of drug or the drug may be introduced in GIT in dissolved or suspended in salivary fluid thereby providing rapid therapeutic action; it offers faster dissolution & absorption of medicament; choking is most common problem faced by dysphagic patients with conventional dosage form hence medicated jelly can serve as better alternative.[4]

In case of drugs with bitter taste and high dosage leads to patient inconvenience. Coating granule or tablet or by formulating as microcapsule cannot provide a solution for masking the taste of the drugs in high dosage formulations. Since this may lead to irritation due to contact of coated medicament with the oral cavity, pharynx may have swallowing difficulty.

Various gelling agents used in preparation of jelly are carrageenan, pectin, agar, sodium alginate, & gelatine. Drugs which are stable in acid condition can only be formulated into jelly using pectin. According to Japanese pharmacopeia medicated jellies are packed in tight containers & in case of preparations that are susceptible to degradation due evaporation of water, low moisture permeability packing or container can be used. These jellies can be stored at room temperature or in cool place.[5]

In the present study, Domperidone is used as model drug. It belongs to the category of antiemetic. It is white powder and is soluble in DMF; sparingly soluble in methanol[6].Domperidone cyclodextrin inclusion complexes were prepared to increase the solubility in aqueous medium.[7] Optimized complex is formulated as jelly and evaluated for various parameters like physical appearance, weight variation, pH, syneresis, drug content and dissolution.

2. MATERIALS & METHODS

2.1 MATERIALS

Table 1: Table showing list of materials with manufacturer

S.NO.	NAME OF THE MATERIAL	MANUFACTURER
1	Domperidone	D. Sharda Pharma Chem Ltd, Gujarat
2	Sucrose	SD-fine chemicals, Mumbai.
3	Xantham gum	SD-fine chemicals, Mumbai.
4	Gelatin	SD-fine chemicals, Mumbai.
5	Citric acid	SD-fine chemicals, Mumbai.
6	Sodium citrate	SD-fine chemicals, Mumbai.
7	Sodium benzoate	Fischer Chemicals, Mumbai.

2.2 CALIBRATION CURVE OF DOMPERIDONE

❖ **Preparation of stock solution:**

About 100mg of domperidone was weighed accurately & dissolved in methanol in a 100ml volumetric flask. The resultant solution had the concentration of 1mg/ml & it was labelled as stock solution

❖ **Preparation of Working standard solution:**

From the stock solution 10 ml was pipette out & diluted to 100ml with 6.8 pH phosphate buffer in a volumetric flask. The resultant solution had the concentration of 100µg/ml & was labelled as working standard solution

❖ **Preparation of serial dilution:**

From the standard stock solution about 0.5, 1.0, 1.5, 2.0, 2.5ml were pipette out in to a series of 10 ml volumetric flask & the volume was made up to the mark with 6.8pH buffer and mixed to obtain solutions in the concentration range of 5, 10, 15, 20, & 25µg/ml of drug. [8, 9]

2.3 PREPARATION OF DOMPERIDONE JELLY

Medicated jelly is prepared by heating & congealing method. Jelly base consisting of sucrose, gelatine & other additives is heated until dissolved then allowed to cool to form jelly.

Steps involved in the preparation of jelly are as follows:

1. Weigh all the required ingredients of the formulation accurately.
2. Sucrose syrup was prepared by adding sucrose to water & is heated until it is dissolved, then citric acid is added to prevent crystallization of sugar
3. Gelatine was soaked in required quantity of water to facilitate its hydration, and then it is added to the above mixture & heated until completely dissolved.
4. Then Domperidone complex, sodium benzoate was dissolved in appropriate vehicle, & added to the above mixture with stirring.
5. After that sodium citrate was added with stirring to maintain pH
6. Then colour, flavour was added & mixed thoroughly.
7. Weight of the jelly was monitored during preparation & the final weight was adjusted to 30g using distilled water, mixed, transferred into

moulds and allowed to cool until it is gelled properly.

8. The formed jelly is packed using gelatine paper & stored in dry place.[10,11]

Table 2: Formulation of Domperidone jelly

S.No.	Ingredients(g)	F1	F2	F3	F4	F5
1.	Optimizeddomperidone cyclodextrine complex	0.216	0.216	0.216	0.216	0.216
2	Sucrose	15	15	15	15	15
3	Xantham gum	2	-	-	-	-
4	Gelatin	-	0.5	1	2	3
5	Citric acid	0.05	0.05	0.05	0.05	0.05
6	Sodium citrate	0.25	0.25	0.25	0.25	0.25
7	Sodium benzoate	0.3	0.3	0.3	0.3	0.3
8	Water	Q.S	Q.S	Q.S	Q.S	Q.S
9	Colour & flavour	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
	Total weight	**30g**	**30g**	**30g**	**30g**	**30g**

Each jelly weighs 5gm & contains 36mg of Domperidone cyclodextrine complex

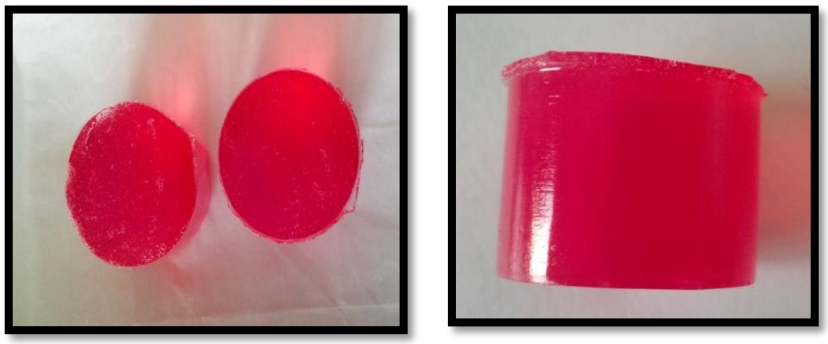

Figure 1: Optimized Jelly formulation

EVALUATION OF FORMULATED JELLIES

1. **Physical examination**
   The medicated jelly was visually evaluated for colour, odour, presence of particulate matter & stickiness. [12, 13]
2. **Weight variation**
   About twenty medicated jellies were taken & their individual weight was determined using analytical balance. Average weight & %weight variation was calculated.[14]
3. **pH:**
   The pH of 1% aqueous solutions of the formulated jellies was determined. About 0.5 gm of jelly formulation was dissolved in 50 ml of distilled water and the obtained pH values were noted.[15, 16]
4. **Syneresis:**
   Syneresis occurs due to lesser concentration of gelling agent & it involves contraction of jelly formulation with release of liquid during storage. All the formulations were stored at room temperature for 24hours & noted for signs of syneresis. Prepared formulations having syneresis were discarded & were not considered in further studies.[1, 5]
5. **Drug content**
   For determination of drug content ten jellies were taken, crushed & gel equivalent to 10mg of Domperidone was dissolved in 100ml of volumetric flask containing 6.8 pH buffer & the final volume was made up to the mark. Then suitable dilution was done & absorbance was taken at 284nm using UV/Visible double beam spectrophotometer. [17]
6. **Dissolution**
   - Dissolution was carried using two different procedures
   - In first procedure dissolution of medicated jelly was carried out using USP II dissolution apparatus (paddle). 900ml of 1.2 pH buffer was taken as dissolution media which was maintained at 37± 0.5°C & the paddle speed was adjusted to 50rpm. 5ml of sample were

withdrawn at 5,10,20,30,45 minutes & replaced with equal volume of fresh buffer. Samples were filtered, diluted & analysed spectrophotometrically at 284nm.[18]

- In second procedure, in order to simulate chewing action medicated jelly was masticated artificially in 6.8 pH buffer for 5mins, during this period samples were withdrawn at 1, 5 minutes & replaced with equal volume of fresh buffer. Then it was transferred into USP II dissolution apparatus containing 1.2pH buffer as dissolution medium with paddle speed of 50rpm. Samples were withdrawn at 10,15,20,25 minutes replaced with equal volume of fresh buffer. Samples were filtered, diluted &analyzed spectrophotometrically at 284nm.[19]

7. Stability studies

Optimized jelly formulation was packed in aluminium foils & stored in high-density polyethylene containers at 30º±2^{0}C/65% RH± 5% for 3months.Samples were evaluated for appearance, pH, syneresis & drug content at the end of each month.[20]

4. RESULTS & DISCUSSION

4.1 STANDARD CALIBRATION CURVE OF DOMPERIDONE

Table 3: Calibration curve data of Domperidone in 6.8pH buffer

S.NO	Concentration (µg/ml)	Absorbance (n=3)
1	0	0
2	5	0.1390±0.002
3	10	0.256±0.006
4	15	0.38±0.004
5	20	0.519±0.007
6	25	0.643±0.016

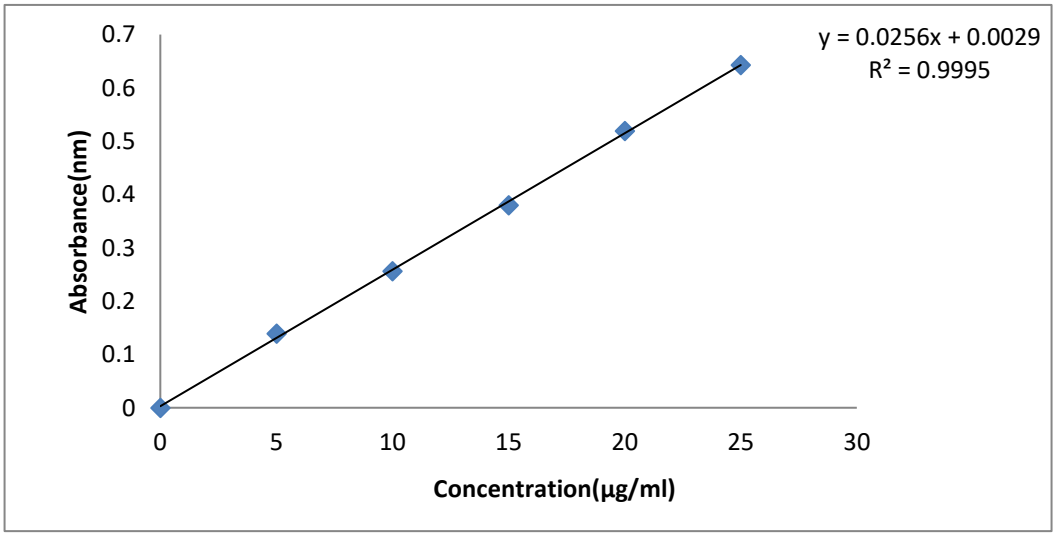

Figure 2: Calibration curve of Domperidone

4.2 RUG EXCIPIENT COMPATIBILITY STUDIES

Shimadzu Fourier-transform infrared spectrophotometer was used to perform the compatibility studies. Absorption bands of pure drug domperidone are as follows:1700-1640 cm^{-1} (C=O stretching),1500-1300 cm^{-1} (C-NHstretching),1200-1000 cm^{-1} (C-N stretching),800-600cm^{-1} (C-Cl bending). It was found that drug & excipients were compatible.

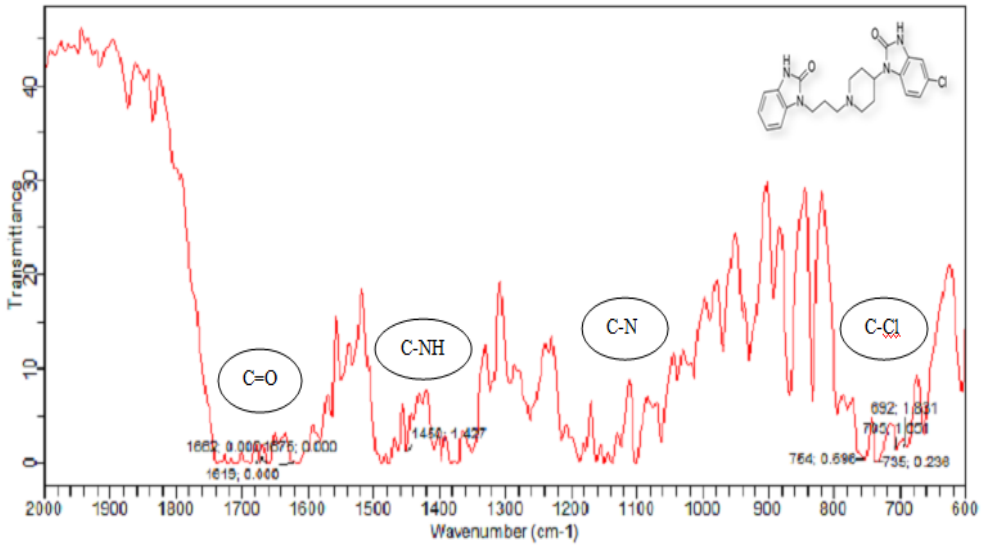

Figure 3: Spectra of Domperidone

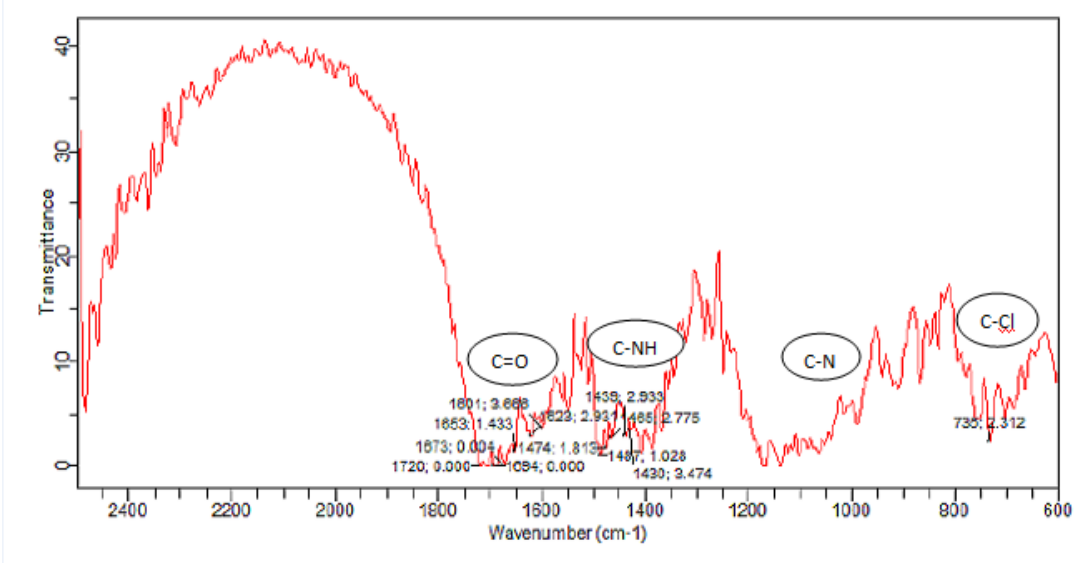

Figure 4: FTIR spectra of drug with excipients used in jelly

4.3 EVALUATION OF MEDICATED JELLY

a. Physical appearance

The F5 formulation was clear, free from particulate matter & non-sticky

Table 4: Physical appearance test parameters

S.no.	Test parameters	F1	F2	F3	F4	F5
1	Clarity	C	C	C	C	C
2	Colour	R	R	R	R	R
3	Odour	PL	PL	PL	PL	PL
4	Particulate matter	N	N	N	N	N
5	Stickiness	S	S	S	SS	NS

C: Clear, R: Red, PL: Pleasant, N: No, S: Sticky, SS: Slight Sticky, NS: Non-Sticky

b. pH

pH of the F5 formulation was found to be 6.83±0.07.

Table 5: pH of formulations

Parameter	F1	F2	F3	F4	F5
pH(n=3)	6.02±0.09	6.31±0.11	6.52±0.17	6.71±0.05	6.83±0.07

c. Syneresis

The F4 & F5 formulation showed no signs of syneresis after 24hours of preparation

Table 6: Syneresis of formulations

Parameter	F1	F2	F3	F4	F5
Syneresis	No	Yes	Yes	No	No

d. Weight Variation

The F4 and F5 formulation showed a % weight variation of 0.28±0.31, 0.21±0.06 which is with in the limit i.e., ±5%.

Table 7: Weight variation of formulations

Parameter	F1	F2	F3	F4	F5
Weight variation (%)	0.78±0.92	0.51±0.26	0.34±0.13	0.28±0.31	0.22±0.15

e. Drug content:

Drug content of F5 formulation was highest i.e. 99.30±0.51% in 6.8 pH buffer

Table 8: Drug content of formulations

Parameter	F1	F2	F3	F4	F5
Drug content%(n=3)	95.98±0.12	97.25±0.31	98.45±0.15	98.75±0.25	99.30±0.51

f. Dissolution

The optimized formulation (F5) showed a drug release of 98.39%with in 25 minutes using simulation method & a drug release of 96.48% in 45minutes using only dissolution apparatus.

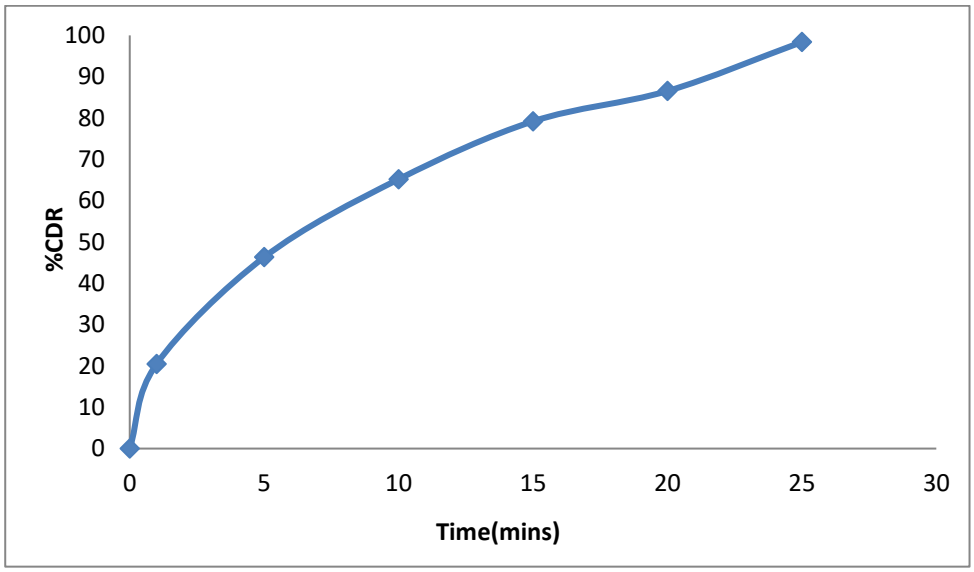

Figure 5: Dissolution profile of F5 formulation by simulation method

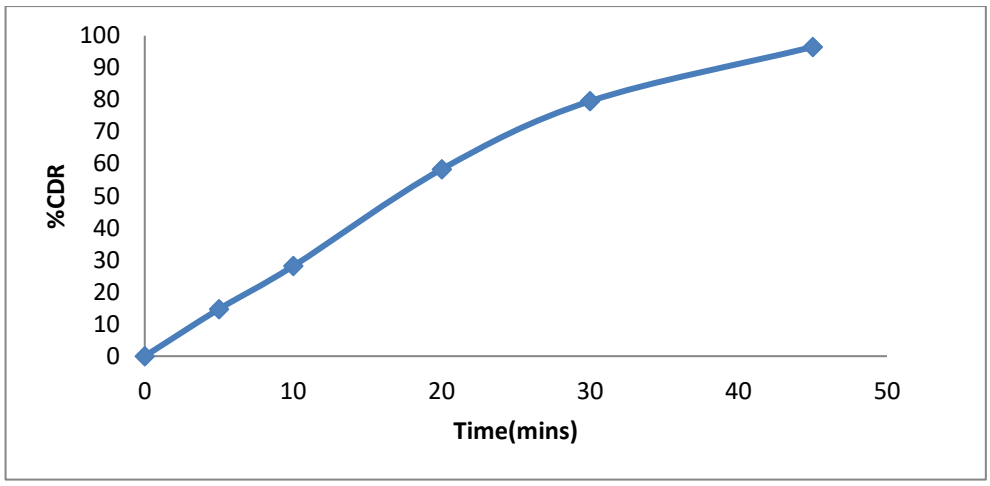

Figure 6: Dissolution studies of F5 formulation using dissolution apparatus

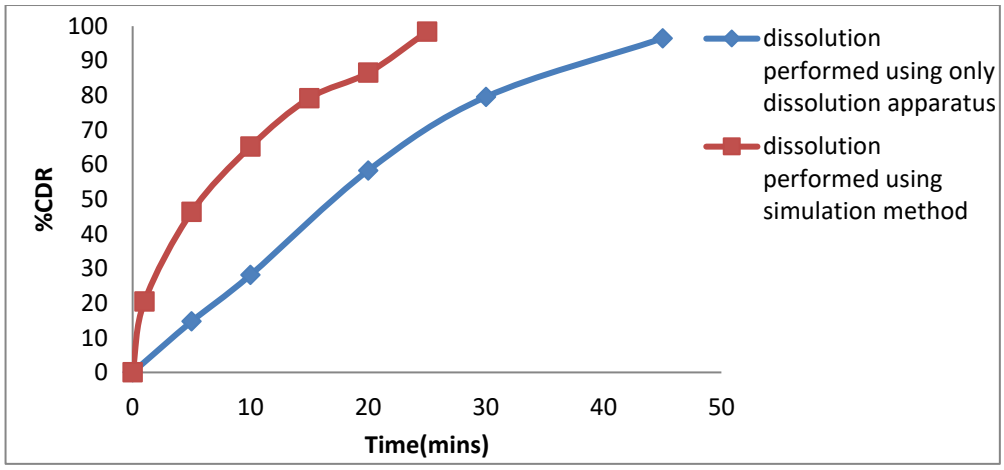

Figure 7: Comparison of dissolution profile of F5 formulation using two different methods

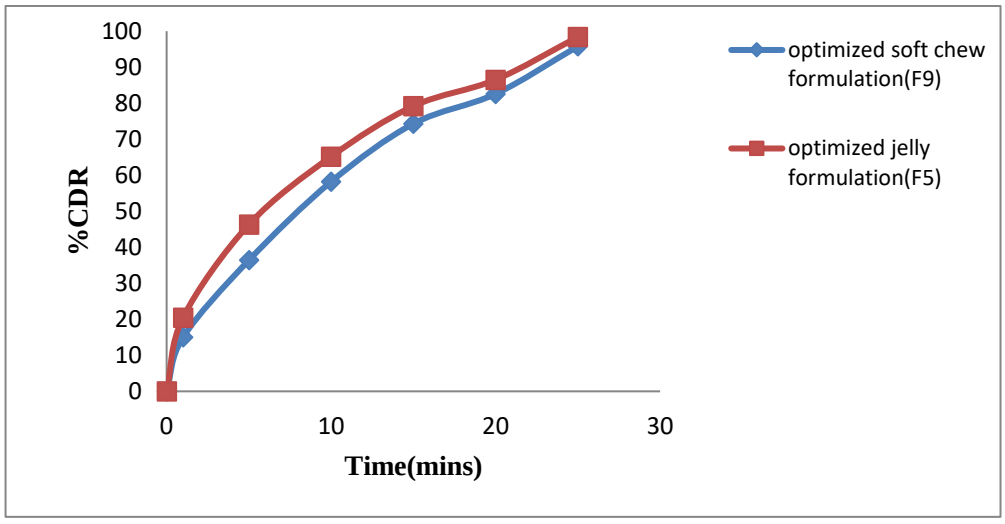

Figure 8: Comparison of dissolution profile of medicated jelly &soft chew formulation

Optimized soft chew formulation showed a drug release of 95.8%, [7] where as F5 formulation of medicated jelly showed a drug release of 98.39% in 25minutes using simulation method, hence, from the following observations it can be concluded that jelly formulation is better than soft chew.

g. Stability studies

Optimized formulation F5 was wrapped in aluminium foil & was stored at $30^0 \pm 2^0$C/65% RH± 5% for 3 months.

Table 9: Stability studies of optimized formulation

S.No.	Stability study period	Appearance	Synergesis	pH	Drug content
1	1month	No change	No	6.83±0.05	99.28±0.02
2	2month	No change	No	6.83±0.34	99.23±0.51
3	3month	No change	No	6.81±0.03	99.17±0.05

5. CONCLUSION

Medicated jelly of Domperidone was formulated. Various formulations of jelly were prepared using Domperidone, sucrose, xantham gum, gelatine, citric acid, sodium citrate, sodium benzoate by heating and congealing method. Among various formulations F4 and F5 formulation has not shown signs of syneresis after 24hr of preparation where as other formulations were prone to syneresis due to lesser concentration of gelling agent. %Drug content of F5 formulation was highest i.e, 99.30±0.51. %Drug release of soft chew & jelly formulation is 95.8% & 98.39% in 25 minutes using simulation method, hence it be concluded that jelly formulation is better compared to soft chew. Optimized formulation was wrapped in aluminium foil and stored at 30º±2ºC/65%RH± 5% for 3months & no significant changes were found during this period.

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