Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2015, 7 (5):80-86
(http://scholarsresearchlibrary.com/archive.html)

Der Pharmacia Lettre
Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Formulation and evaluation of medicated chewing gum of Ondancetron HCl for chemotherapy induced nausea and vomiting

Prabhanshu Vaishya, Ashwani Mishra and Anupam Pathak

Department of Pharmacy, Barkatullah University, Bhopal

ABSTRACT

Medicated chewing gum is an excellent drug delivery system for self medication as it is convenient and can be administered discreetly without water. They can be used for the treatment of mouth diseases or systemic absorption through oral mucosa. Medicated chewing gum contains masticatory gum base along with pharmacologically active ingredient which is intended to chew not to be swallowed. Available data suggest that the world market for chewing gum is approximately 560,000 tons, which represents approximately US $5 billion annually. One piece of chewing gum weighs, on average, 1.5 g, and some 374 billion pieces are sold worldwide every year. Medicated chewing gums were prepared by Compression method .PVP, PVA, beeswax, dextrose, calcium carbonate, peppermint, ascorbic acid, Polyethylene glycol 400 and Ondancetron Hcl were used in the formulation in different concentration .Formulations were subjected for following evaluation Weight variation , Friability , Texture analysis & In vitro dissolution studies. Best promising formulation was selected and it was found to be formulation batch FR4 which showed gumminess 8126.33, chewiness 6144.29 and resilience 0.725 among all prepared formulation.

Key words: Gumminess, Chewiness, Resilience, friability.

INTRODUCTION

Medicated chewing gum is an excellent drug delivery system for self medication as it is convenient and can be administered solely without water. Medicated Chewing Gum is a single solid dosage form novel drug delivery system which is intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa. Medicated chewing gum contains masticatory gum base along with pharmacologically active ingredient which is intended to chew not to be swallowed. [1][2]

Medicated chewing gum has number of advantages like It does not require water to swallow. Hence it can be taken anywhere at any time, Advantageous for those patients having difficulty in swallowing, Counteracts dry mouth, prevents candidiasis and caries, Highly acceptable by children and adults ,Maximum drug absorbed from oral mucosa thus avoids first pass metabolism and increases the bioavailability of drugs, Neutralizes plaque acids that form in the mouth after eating fermentable carbohydrates, Stimulates flow of saliva in the mouth and Fast onset of action due to rapid release of drug in oral cavity and subsequent absorption in systemic circulation.[3] [4]

Ondansetron HCl is used as drug because it exhibits half life of 5 hrs. It is sparingly soluble in water. Absorption through oral cavity is good.[5-11] .It is majorly used in treatment of chemotherapy induced nausea and vomiting.

After analysing and studying about drug and dosage form, formulation of medicated chewing gum of ondansetron HCl was decided by using combination of polyvinyl pyrollidone and polyvinyl alcohol as gum base. Polyethylene glycol was used as a plasticizer to impart chewability and gummy texture to the formulation.

MATERIALS AND METHODS

Ondansetron HCL obtained from Mariya Pharmaceuticals, Indore, India. Polyvinylpyrrolidone, polyvinyl alcohol, Polyethylene glycol 400, beeswax, dextrose, calcium carbonate, peppermint, ascorbic acid (CDH (P) Ltd, New Delhi and other reagent were of analytical grade.

Formulation of directly compressible mixture
First polyvinylpyrrolidone, polyvinyl alcohol 200, beeswax, dextrose, calcium carbonate, peppermint, ascorbic acid and drug are weighed separately and mixed in ascending order in a mortar. After mixing, ingredients thoroughly grounded in a mortar pestle and then required quantity of PEG 400 was added. Then the whole mixture was mixed and ground thoroughly using a pestle mortar . After mixing and grinding the mixture was subjected for compression by using rotary tablet press compression machine to form medicated chewing gum as shown in Table no1

Evaluation
Evaluation of flow property of mixture
1 Bulk density and tapped density
Directly compressible blend was poured gently through a glass funnel into a graduated cylinder of bulk density apparatus. Then Bulk density and tapped density were calculated.

$$Bulk\ density = \frac{Weight\ of\ sample\ in\ gram}{Final\ volume\ of\ sample\ contained\ in\ cylinder}$$

$$Tapped\ density = \frac{Weight\ of\ sample\ in\ gram}{Final\ volume\ after\ tapping\ in\ cylinder}$$

2 Carr's compressibility index
Used for compare the bulk density and tapped density.
The Compressibility index was calculated by the formula

$$Tapped\ density = \frac{Tapped\ Density\ -\ Bulk\ Density}{\text{TappedDensity}}$$

3 Hausner ratio
The flow properties of blend, granules or Powder are measured by this ratio.

$$Hausner\ ratio = \frac{\text{BulkDensity}}{\text{TappedDensity}}$$

4 Weight Variation : Twenty chewing gums were selected at random and the average weight was calculated. The batch passes the test if not more than two of the individual chewing gums weight deviates from the average weight by more than the acceptable percentage .shown

5 Friability:
Chewing gums were weighed and placed in the Roches friabilator. The chewing gums were placed into the apparatus for four minutes, which was rotating at the speed of 25 revolutions/min.Then the chewing gum were removed and de dusted and weighed. The Percentage loss in weight was calculated and taken as a measure of friability. Ideally there should not be more than 1% variation of weight loss .

$$\text{Percent } Friability = 1 - \frac{Loss\ in\ weight}{Initial\ Weight} \times 100$$

6 Texture analysis:
Texture analysis was performed by stable micro system TA.XD texture analyser .In that the heavy duty platform was placed on the machine base. The sample was positioned on the platform, centrally under the probe. Then the probe approaches the sample and once the 5g trigger force is attained, a rise in force is observed, as the probe penetrates through the chewing gum. A drop in force is observed when the probe enters the interior of the gum. The probe returns to its original starting position when a penetration distance of 3mm from the trigger point is reached.

The peak force is measured as an indication of the hardness. The force value at the distance of 1.5mm is considered as the interior hardness.

7 In vitro study:
In vitro study was performed on modified dissolution apparatus by taking a medicated chewing gum in the receptor compartment and then it was subjected for a number of compression cycle of 40 to 50 times per minute**.** Then aliquot was collected at a regular interval of 5 minutes for 30 minutes. Then drug concentration was determined by UV spectroscopy.

8 Differential scanning calorimetry of ondancetron HCl
Differential Scanning calorimetry study was performed by using Pyris 6 DSC(Jade) instrument.The DSC thermogram of ondancetron HCL were generated and investigated for presence of peaks. The DSC was performed by the instrument Pyris 6 DSC (Jade). The temperature range was taken from 0°c to 350°c. The endothermic peak revealed the melting point of samples between 188 to 193°c which can be used as a test for purity analysis and also for sample characterization. The peak was observed between 188 to 193°c. This shows the drug melts in between 188 to 193°C.

RESULTS AND DISCUSSION

Prepared mixture was evaluated for their flow properties. Carr's compressibility index obtained was ranged from 13.09 to 16.90 as shown in table no. 7.5 which show good flow properties. Hausner ratio was observed in the range of 0.85 to 0.86 as shown in table no 4These values shows good flow properties of prepared mixture.

Weight variation
Weight variation was calculated by using 20 chewing gums. The results of weight variation as shown in table no. 3 & 4 were found to be passed.

Table no. 1: Formulation of trial batches of chewing gum placebo using various concentrations of ingredients

S.No	Ingredients	F1	F2	F3	F4	F5
1	PVP (mg)	6000	6000	-	-	-
2	PVP+PVA 1 : 1 (mg)	-	-	6000	6000	6000
3	PEG 400 (ml)	0.6	1	0.4	0.6	0.8
4	Calcium carbonate (mg)	480	480	480	480	480
5	Beeswax (mg)	580	580	580	580	580
6	Dextrose (mg)	540	540	540	540	540
7	Peppermint (mg)	80	80	80	80	80
8	Ascorbic acid (mg)	16	16	16	16	16

S.No	Ingredients	F6	F7	F8	F9	F10
1	PVP(mg)	-	-	-	-	-
2	PVP+PVA 1 : 1 (mg)	6000	6000	6000	6000	6000
3	PEG 400 (ml)	1	1.2	1	1	1
4	Calcium carbonate (mg)	480	480	400	420	440
5	Beeswax (mg)	580	580	580	580	580
6	Dextrose (mg)	540	540	620	600	580
7	Peppermint (mg)	80	80	80	80	80
8	Ascorbic acid (mg)	16	16	16	16	16

Table no 2: Evaluation of trial batches of chewing gum placebo using various concentrations of ingredients

S. No.	Test	F1	F2	F3	F4	F5
1	Friability	Fail	Fail	Pass	Pass	Pass
2	Weight variation	Pass	Pass	Pass	Pass	Pass

Table no. 3: Formulation of trial batches of chewing gum placebo using various concentrations of ingredients

S. No.	Test	F6	F7	F8	F9	F10
1	Friability	Pass	Pass	Fail	Fail	Fail
2	Weight variation	Pass	Pass	Pass	Pass	Pass

Friability test
Friability test was performed using 16 chewing gums from each batch. The results of F1 F2 F8 F9 and F10 batches were out of the passable limits among placebo formulations but all the Drug entrapped formulation showed friability in acceptable range .

Table no. 4: Formulation of trial batches of chewing gum with incorporation of drug using various concentrations of ingredients

S.No	Ingredients	FR1	FR2	FR3	FR4	FR5
1	PVP+PVA 1 : 1 (mg)	6000	6000	6000	6000	6000
2.	Ondancetron HCl (mg)	100	100	100	100	100
3.	PEG400 (ml)	0.4	0.6	0.8	1	1.2
4.	Calcium carbonate (mg)	480	480	480	480	480
5.	Beeswax (mg)	580	580	580	580	580
6.	Dextrose (mg)	540	540	540	540	540
7.	Peppermint (mg)	80	80	80	80	80
8.	Ascorbic acid (mg)	16	16	16	16	16

Table no 4: Evaluation of drug entrapped formulation of chewing gum

Batch No.	Bulk density (g/cm3)	Tapped density (g/cm3)	Carr's compresibility index (%)	Hausner ratio (HR)
FR1	0.133	0.153	13.06	0.86
FR2	.0.133	0.153	13.06	0.86
FR3	0.133	0.153	13.06	0.86
FR4	0.142	0.166	16.90	0.85
FR5	0.142	0.166	16.90	0.85

Table no 5 Weight variation and percentage Friability of Prepared formulation batches.

Batch No.	Weight variation	% Friability
FR1	Passed	0.39
FR2	Passed	0.14
FR3	Passed	0.26
FR4	Passed	0.12
FR5	Passed	0.13

Table no 6 Adhesiveness, Springiness, and Cohesiveness of chewing gum

S. No.	Adhesiveness ± SD (g/sec)	Springiness ±SD	Cohesiveness ±SD
FR3	-3.264 ± 0.5	0.632 ± 0.8	0.634 ± 0.2
FR4	-2.535 ± 0.5	0.756 ± 0.8	0.650 ± 0.2
FR5	-2.216 ± 0.5	0.593 ± 0.8	0.596 ± 0.2

Table no.7: Gumminess, Chewiness, Resilience of chewing gum

S. No.	Gumminess ±SD	Chewiness ±SD	Resilience ±SD
FR3	7683.96 ± 816.9	4857.67 ± 1134.3	0.683 ± 0.07
FR4	8126.33 ± 816.9	6144.29 ± 1134.3	0.725 ± 0.07
FR5	6542.97 ± 8.619	3882.64 ± 1134.3	0.589 ± 0.07

Table No 8 Cumulative percent drug release of Formulation FR4

Time (min)	%CDR
0	0
5	12.3
10	17.6
15	20.1
20	22.1
25	25.8
30	28.28

Texture analysis

Texture analysis was performed for only drug entrapped formulation FR3 ,FR4 and FR5 The gumminess, adhesiveness, springiness, cohesiveness, resilience and springiness of formulation FR4 was found to be best in comparison to FR3 and FR5 and the result as shown in table no 6 and table no. 7 was found to be acceptable.

In vitro drug release study

The In vitro drug release was carried out for formulation FR4 as its % friability and weight variation is less then FR1, FR2, FR3 and FR5. Also the gumminess, springiness cohesiveness, chewiness, resilience and adhesiveness of formulation FR4 is good as compare to FR3 and FR5. From the drug release study showed that the maximum drug release observed was 28.28 % in 30 minutes.

Study through Differential Scanning Calorimeter

The DSC thermograms were obtained and investigated to check the interaction between the drug and the polymer. The DSC was performed by the instrument Pyris 6 DSC (Jade). The temperature range was selected to observe

thermogram was 0ºc to 350ºc. The endothermic peak reported in Fig no 1 95 ºC to 99 ºC was the phase transition of Drug ,One more sharp endotherm was observed between 188ºC to 193ºC shows melting point of drug in thermogram. In Figure no 2 a sharp endothermic peak were observed at 55 ºC this could be because of presence of low melting point substances like bees wax, peppermint and dextrose Some other endothermic peaks where also observed at 100ºC and 125ºC this could be because of the polymer polyvinylpyrrolidone and Poly vinyl Alcohol Which shows melting point in these temperature ranges. One sharpe endothermic peak was observed between 175ºC to 190ºC which showed melting point of drug. The result obtained from DSC study revealed that drug didnot potentially bound to the polymer which could affect its desired pharmacological action as the endotherm in figure no 2 thermogram of the formulation showed the melting point of drug between 175ºC to 190ºC .

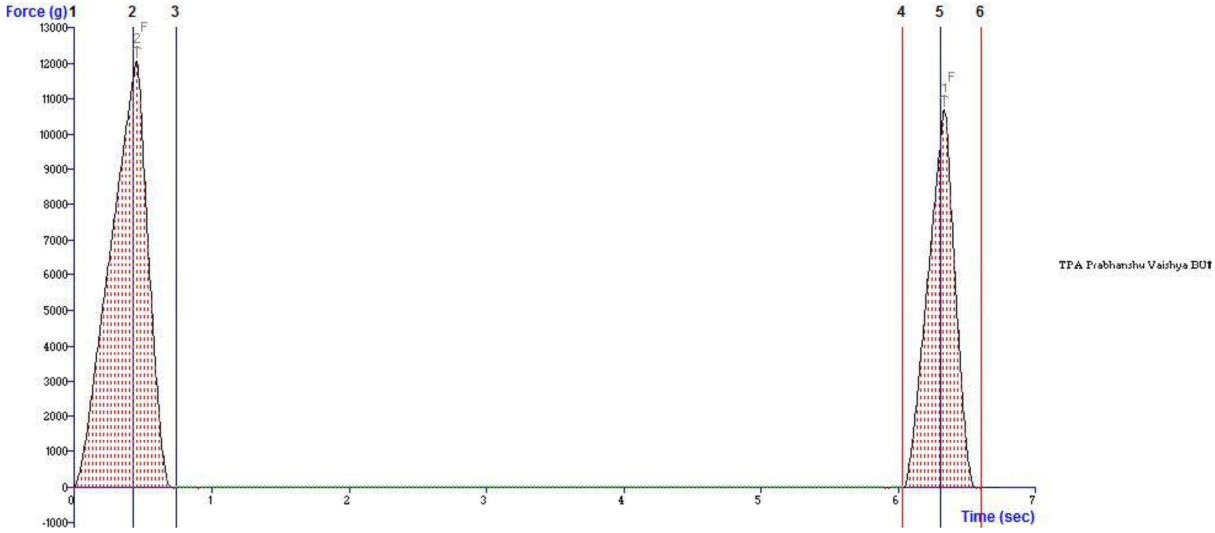

Figure no 1: TPA curve of FR3

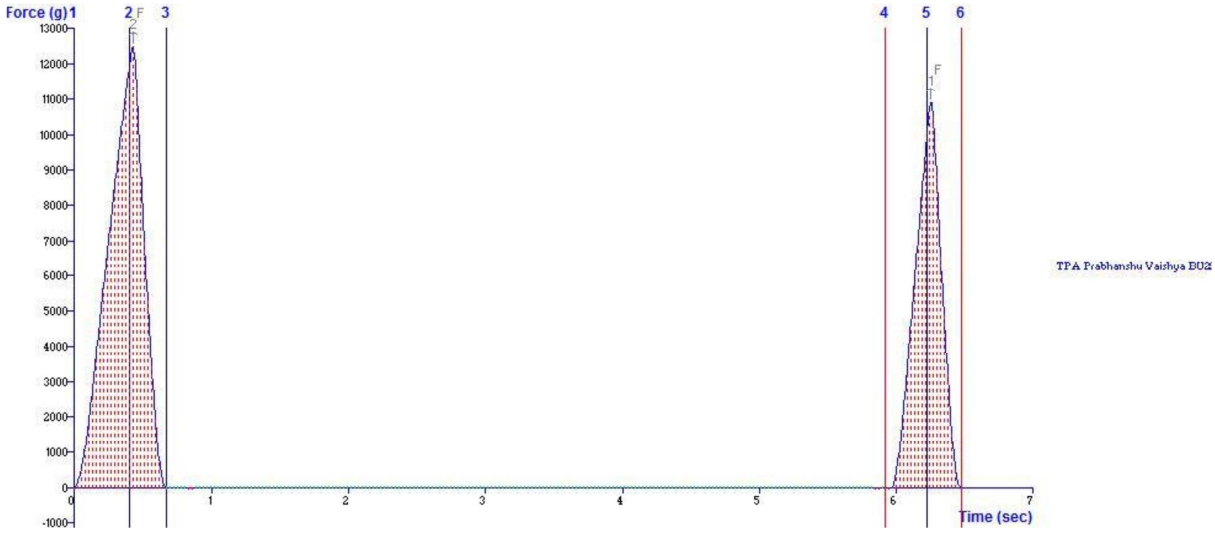

Figure no 2 TPA curve of FR4

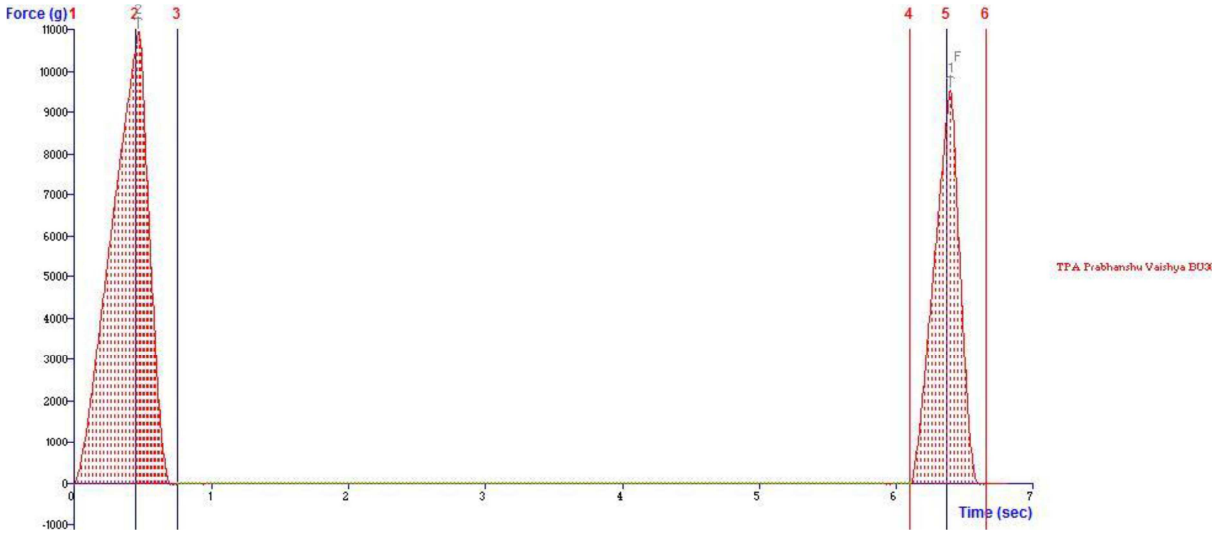

Figure no 3: TPA curve of FR5

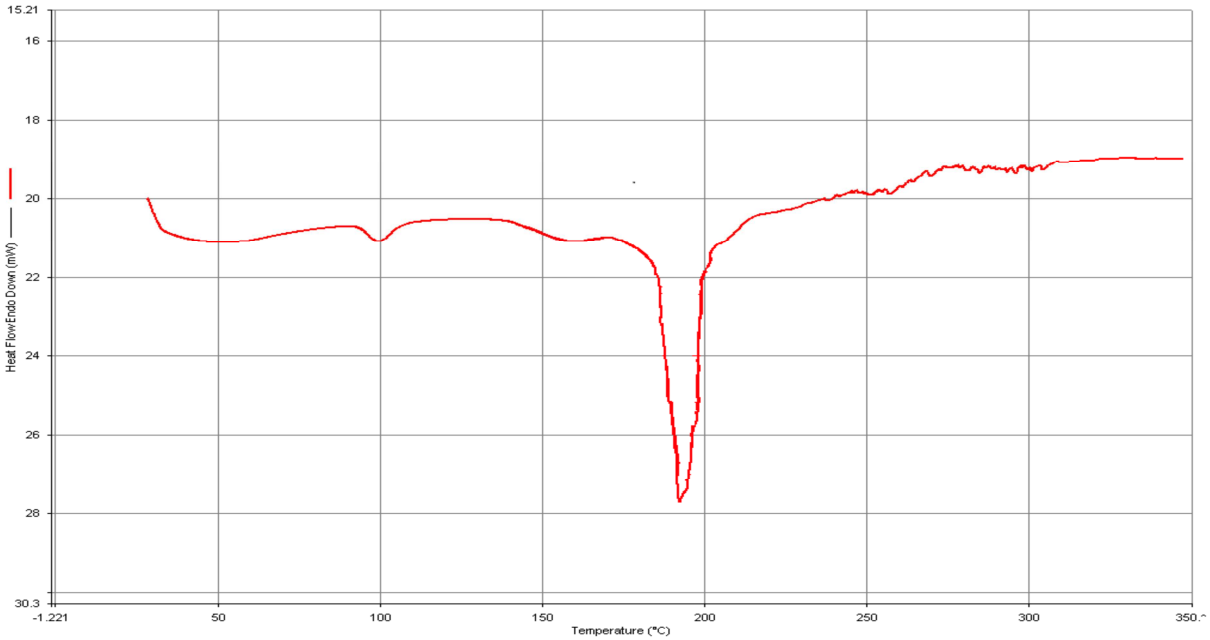

Fig no 4 Differential Scanning calorimeter study of Pure drug

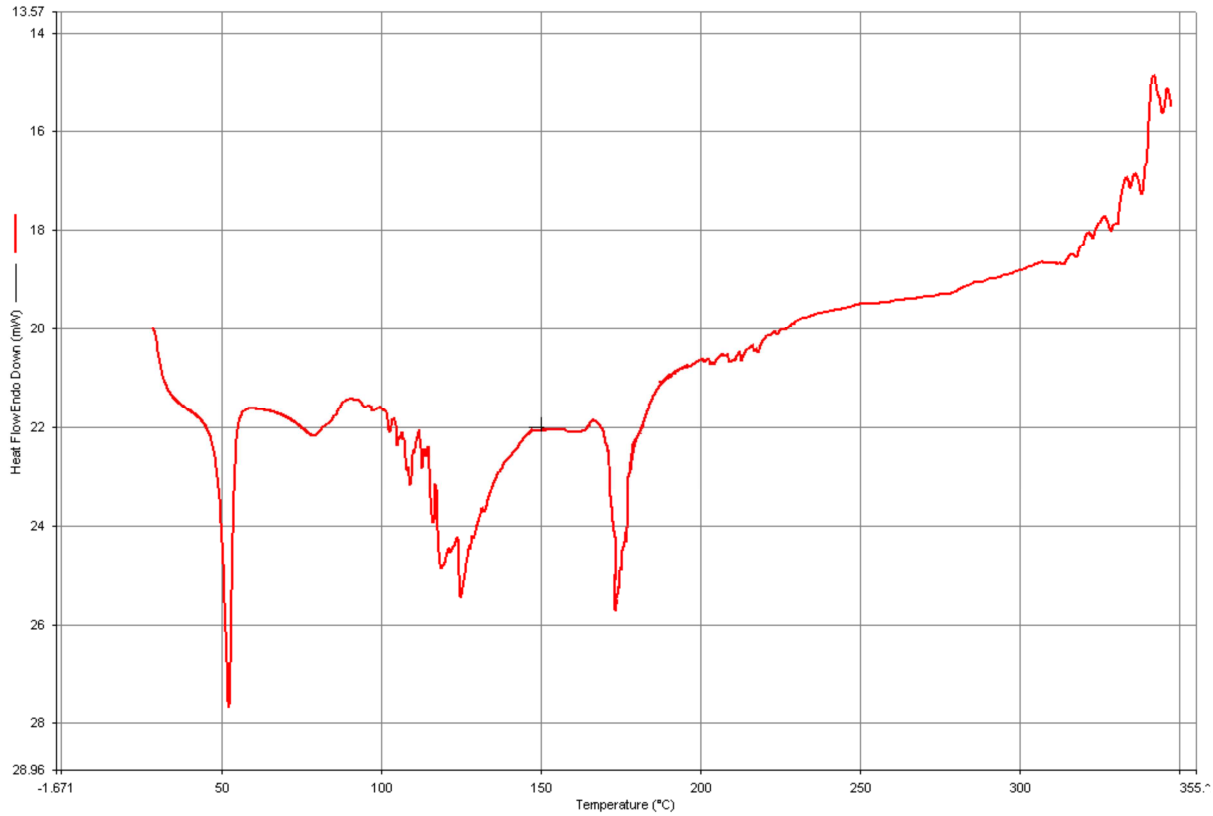

Fig no5 Differential Scanning calorimeter study of optimized formulation

CONCLUSION

Medicated chewing gum of Ondansetron HCl was successfully prepared by direct compression technique. The formulation FR4 shows good flow properties of prepared mixture. The hausner ratio and carr's index shows good flowing of the mixture. The weight variation, % friability of formulation F4 was found to be in the acceptable limiting and thus passed this evaluation parameters. The texture analysis results shows that the FR4 shows good gumminess, adhesiveness, springiness, cohesiveness, resilience and springiness as compared to FR3 and FR5 and it is also in the acceptable limit. The in vitro study of Formulation shows the release of 28% of drug from the formulation in 30 minutes. Therefore medicated chewing gum of Ondansetron prepared will be possibly beneficial for immediate and continuous release of drug and thus it is promising dosage form for future aspect.

REFERENCES

[1] Sharma N. *Am J Ph Res*, **2013**, 4, 19-27.
[2] J Jacobsen; L L Christrup .*Am J Drug Del*, **2004**, 2,75-85 .
[3] T Imfeld. *Cri Rev Ora Bio Med*, 10, 3, 405-419.
[4] L Maggie; H Segale; S Conti; M E Ochea; A S Conte. *Eur J Ph Sci*, **2005**, 2, 4, 487-493.
[5] S S Malke; S S Sidhya; A S Desai; V J Kadam . *Ind Drugs*, **2006**, 43, 3, 191-198 .
[6] Y Morjaria ; W J Irwin ;P X Barnett ;R S Chan ;B R Conway . *DDT*, **2004**, 12 – 15.
[7] R C Rowe R. *Drug Discov Tod*, **2003**, 8, 58-71.
[8] L C Kvist ;S B Andersson ; J Berglund ;B Wennergren ;S M Fors .*J Ph Biomed Ana*, **2000**, 4, 405–411 .
[9] K Ezhumalai;P Ilavarasan .*Int J Ph Tech* ,**2011**, 3,1, 725-744 .
[10] K A Ly; P Milgrom . *J Ama Dent Assoc*, **2008**, 139, 5, 553-563.
[11] H Naik; S Gupta S.*Int J Ph Res Dev*, **2010**, 2, 8, 66-76.