World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Original Article

Comparative study of formulations of ondansetron hydrochloride orodispersible tablets by effervescent and sublimation methods

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Received: 10-09-2014 / Revised: 23-09-2014 / Accepted: 26-09-2014

Abstract

In the present work orodispersible tablets of Ondansetron hydrochloride were formulated by effervescent and sublimation method using factorial design. In the effervescent method, crospovidone (1.31%-4.68%) was used as superdisintegrant whereas citric acid (7.95%-18.04%) and sodium bicarbonate (5.22%-28.77%) were used as effervescent agent. In the sublimation method, crospovidone (1.58%-4.41%) was used as superdisintegrant whereas camphor (6.34%-17.35%) was used as subliming agent. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, disintegration time and *In Vitro* drug release pattern. Total 15 batches were formulated by effervescent method and 9 batches were formulated by sublimation method. Disintegration time of the formulations prepared by effervescent method was found between 13-36 secs whereas formulations prepared by sublimation method showed disintegration time between 7-39 secs. Among all the formulations, the formulation (S6) prepared by sublimation method using crospovidone 4% and camphor 8% was found to have the minimum disintegration time (7 seconds). Finally, it was concluded that Orodispersible tablet of Ondansetron Hydrochloride can be successfully formulated using effervescent and sublimation method and can be used as a novel drug dosage form for pediatric and geriatric with improved patient compliance and enhanced bioavailability.

Keywords: Orodispersible tablet, Ondansetron hydrochloride, crospovidone, citric acid, sodium bicarbonate, camphor

INTRODUCTION

ODTs are the solid unit dosage forms/entities containing medicinal substances which disintegrate or dissolve rapidly in oral cavity usually within a few seconds even without the need of water or chewing [1]. The European Pharmacopoeia defines "Orodisperse as a tablet that can be placed in the mouth where it disperses rapidly before swallowing" [2]. Recently European Pharmacopoeia has used the term orodispersible tablet for tablet that disperse readily and within 3 minutes in mouth before swallowing [3]. United States of America food and drug administration (FDA) defines "ODT as a solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon a tongue" [4]. ODTs are also known as orodispersible tablets, mouth dissolving tablets, rapimelts, melt-in-mouth tablets, fast disintegrating tablets and rapid dissolving tablets. As the tablet disintegrates in mouth, this can enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx and esophagus. In such cases, bioavailability of drug is significantly enhanced by avoiding first pass hepatic metabolism than those observed with conventional tablets. ODTs also combine the advantages of both liquid and conventional tablet formulations allowing the ease of swallowing in the form of liquid. The advantages of these dosage forms are continuously and increasingly being identified in both pharmaceutical industries as well as in academia [1]. Ondansetron HCl is a potent antiemetic drug indicated for the treatment and/or prophylaxis of postoperative and chemotherapy or radiotherapy induced emesis and also used in the early onset of alcoholism. In general, emesis is preceded with nausea and in such condition it is difficult to administer drug with a glass of water; hence it is beneficial to administer such drugs as ODTs. Also, the performance of ODTs depends on the technology used in their manufacture. The orally

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disintegrating property of these tablets is attributable to the quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration [5]. So far, various techniques have been developed based on different principles and the selection of appropriate technique is necessary. Thus, in the present study an attempt has been made to formulate ODT of Ondansetron HCl with good mouth feel so as to prepare a "patient-friendly dosage form" and to compare the effectiveness of the methods employed for the formulation of Ondansetron HCl (effervescent method and sublimation method).

MATERIALS AND METHODS

Materials: The drug molecule Ondansetron Hydrochloride was received as gift sample from Lomus Pharmaceuticals Pvt. Ltd. Other materials like microcrystalline cellulose, crosprovidone, magnesium stearate, purified talc, were also obtained from Lomus Pharmaceuticals Pvt. Ltd. Sodium bicarbonate, Hydrochloric acid, camphor, mannitol were obtained from Research Laboratory of National Model college for Advanced Learning.

Methods

Determination of λmax: Weighed amount of Ondansetron Hydrochloride was dissolved in 0.1N HCl to obtain a 1000mcg/ml solution. This solution was subjected to scanning between 200 – 400 nm and absorption maximum was determined.

Preparation of standard calibration curve in 0.1N HCl: A stock solution of standard Ondansetron Hydrochloride of 100µg/ml concentration was prepared in 0.1N HCl. The stock solution was then used to prepare the standard working solution of five different concentrationsof 2, 4, 6, 8and 10µg/ml respectively. The absorbance of each sample solution was measured at 310nm using 0.1N HCl as a blank and calibration curve with absorbance vs concentration was plotted.

Preparation of 0.1 M Hydrochloric acid (HCl): Eight and half milliliter of concentrated HCl was diluted to 1000ml with purified water to prepare 0.1 M HCl solution.

Fabrication of tablet: The effects of excipients were studied in trial batches. Total 8 trial batches were formulated to determine the formulation and to obtain the range of concentration of excipients needed to achieve the desired DT. Initially, croscarmellose was used as superdisintegrant but since our objective of rapid disintegration was not met it was replaced by crospovidone. A study also shows that crospovidone was significantly superior to other superdisintegrants and exhibits lowest disintegration time [6]. This may be due to the fact that crospovidone exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels. The concentration of magnesium stearate, talc and saccharin was also reduced which helped to obtain considerable DT.A study has also revealed that a combination of magnesium stearate and talc in higher concentration may not be useful as a lubricant in particular situations where a lower disintegration time is required, but may be useful in situations where a higher crushing strength and disintegration time is required e.g. in sustained release tablets [34]. This may be due to the hydrophobic nature of magnesium stearate and talc which retards the penetration of aqueous medium. With all these findings, the final optimized batches were designed by central composite design. Three additional batches were formulated using crospovidone alone, by direct compression method, in different concentration to study the effect of same as super-disintegrant. Total 15 batches were prepared by effervescent method and 9 batches by sublimation method using factorial design. Batch size of each formulation was of 100 tablets and weight of each tablet was 200 mg. The flow chart of tablets prepared by effervescent method and sublimation method is shown in Annex I and II. The composition of final batches prepared by effervescent method and sublimation method is shown in Annex I and II.

Preparation of orodispersible tablet of ondansetron hydrochloride by effervescent approach: MCC PH-101, crospovidone, mannitol and other ingredients were sieved through sieve no. 30 and lubricants were sieved through sieve no. 120. MCC PH-101 was mixed with mannitol. Ondansetron HCl was then geometrically mixed with mixture of MCC PH-101 and mannitol. The powder so obtained was dried in hot air oven then mixed with citric acid, sodium bicarbonate and crospovidone and then was finally mixed with lubricants in the polybag for 5 minutes. Compression was performed using 10 station rotary compression machine with 8mm round punches.

Preparation of orodispersible tablet of ondansetron hydrochloride by sublimation approach: Preparation method was similar to that of effervescent method, only difference was in the formulations aspect where the sublimating agent (camphor) was used along with superdisintegrants. Sublimating agent used was triturated prior to use and was then passed through sieve no 30. Prepared powder was then compressed. The prepared tablets were then subjected to the hot air oven for sublimation of camphor for 6 hrs.

Evaluation of orodispersible tablets of ondansetron hydrochloride [7]: Tablets were evaluated for their physicochemical parameters such as weight variation, thickness, hardness, friability, content uniformity, disintegration time, wetting time and *In-Vitro* dissolution.

Weight variation: Twenty tablets were randomly selected and weighed individually to determine the weight variation. The result was expressed as average weight± standard deviation.

Thickness: Ten tablets were randomly selected and thickness was measured using digital vernier calipers. The result was expressed as average thickness ± standard deviation.

Hardness: Six tablets were randomly selected and hardness was measured using monchanto hardness tester. The result was expressed as average hardness ± standard deviation.

Friability: Twenty tablets from each batch were selected randomly and were weighed. The tablets were transferred to friability test apparatus which was operated at 25 rpm for 4 minutes or up to 100 revolutions [5]. **Content uniformity [8]:**

Standard preparation: Ondansetron HCL reference standard (0.1g) was weighed accurately. The drug was dissolved in 0.1N HCL and volume was made upto 100 ml with the same solvent. Then 10 ml was diluted to 100 ml with the same solvent.

Sample preparation: Three tablets were selected randomly from each batch and were weighed. Each tablet was taken in 100ml volumetric flask and dissolved in 0.1N HCl. It was sonicated for 5 minutes. The volume was then maintained up to 100ml using 0.1N HCl. From the resulting solution 10ml was taken and diluted upto 100ml. The absorbance of this final solution and standard ondansetron HCl solution were compared at wavelength 310 nm using 0.1N HCl as a blank using uv-visible spectrophometer.

Wetting time: A glass Petri dish was partially filled with waterand a tablet was placed on the surfaceofa band of filterpaper.The uptake of wateroccurs from the lower surface of the tablet. The timerequired for water to reach the center of the uppersurfaceof the tablet was noted as wetting time.

Disintegration time: The time required for disintegration of six tablets was determined by placing tablets in each tube of disintegration test apparatus (USP) without disc plates containing 900 ml of distilled water. Temperature was maintained at 37± 2°C. Time was noted when all tablets passed through the sieve.

Dissolution test: For dissolution test method given in USP had followed. In Vitro releases of Ondansetron HCl orodispersible tablets were carried out in a six basket dissolution test apparatus with the following conditions [9].

Medium: 0.1NHCL
Volume: 500ml
Apparatus: II (paddle)
RPM: 50
Time: 10 minutes

After 10 minutes, the sample was withdrawn and filtered through a whatman filter paper. Absorbance of each filtrate sample was measured and compared with 10 µg/ml standard solution using uv-visible spectrophotometer (λ max; 310 nm). 0.1 N HCl was used as a blank.

RESULTS AND DISCUSSIONS

Calibration curve: Calibration curve were prepared by plotting graph of concentration versus absorbance for a concentration of 2, 4, 6, 8 and 10µg/ml of ondansetron HCl reference standard in 0.1 N HCl at 310nm. The correlation coefficient (R^2) value of ondansetron HCl standard in 0.1N HCl was found to be 0.999. The plotted calibration curve for ondansetron HCl reference standard in 0.1N HCl is given in Figure 1. The regression analysis for calibration curve showed very good correlation (R^2 = 0.999) for all the curves at the wavelength 310 nm in 0.1 N HCl, showing that the method of analysis of ondansetron hydrochloride by UV spectrophotometer was suitable. The analysis for calibration curve showed that the solvent used had no interference while taking absorbance of the drug in UV spectrophotometer at 310 nm.

Optimization of formulation using central composite design: The solid lines in the contour plot indicate the lower disintegration time i.e. 10 seconds and the broken line indicate the higher disintegration time i.e. 15 seconds. To formulate the optimized batch of ondansetron hydrochloride orodispersible tablet with disintegration time between 10-15 seconds, the various combinations of concentration of crospovidone and camphor in the white area between solid and the broken lines may be selected as shown in figure 7. The optimization of composite responses of two variables indicates that with the increase in concentration of both camphor and crospovidone the disintegration time decreases but the effect is more pronounced in case of crospovidone. The plot also shows that when our target disintegration time is of 10 seconds, the combination of concentration

of two variables should be camphor around 7.32% and crospovidone around 4.41% as in figure 2.

The solid lines in the contour plot indicate the lower disintegration time i.e. 12 seconds and the broken line indicate the higher disintegration time i.e. 15 seconds. To formulate the optimized batch of ondansetron hydrochloride orodispersible tablet by effervescent method with disintegration time between 12-15 seconds, the various combinations of concentration of sodium bicarbonate and citric acid in the white area between solid and the broken lines may be selected, the concentration of crospovidone being constant i.e. 3% w/. The optimization of composite responses of three variables indicates that with the increase in concentration of both citric acid and crospovidone the disintegration time decreases. In case of sodium bicarbonate initially disintegration time increases with increasing concentration of sodium bicarbonate. Later, with the increase in concentration of sodium bicarbonate disintegration time decreases gradually. The plot also shows that when our target disintegration time is of 10 seconds, the combination of concentration of three variables should be citric acid around 16.25%, sodium bicarbonate around 28.77% and crospovidone 4.68% as depicted by figure 3.

Evaluation of orodispersible tablets of ondansetron hydrochloride: Tablets were evaluated for their physicochemical parameters such as weight variation, thickness, hardness, friability, content uniformity, disintegration time, wetting time and In-Vitro dissolution.

Weight variation: Compressed tablets from different formulation had uniform weight due to uniform die fill which were within acceptable limit i.e. % deviation was within ±7.5% as per USP. The result suggests that all the formulations had free flowing property. As crushing strength directly effects wetting and disintegration of tablet, formulated mixture for both effervescent method and sublimation method had been compressed maintaining hardness between 2 kg/cm^2-4 kg/cm^2. The average weights of all the formulation are listed in table 3 and 4.

Thickness: Tablet mean thicknesses were found to be almost uniform in all the formulations and were found to be in the range of 3.64mm to 4.05mm. The average thicknesses of all the formulation are listed in table 3 and 4.

Friability: Friability was determined to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting. The results are listed in table 3 and 4. The average friability for all the formulations was between 0.23%- 0.95% which was found to be within the limit (i.e. maximum 1%). The friability of formulations prepared by sublimation method is higher than those prepared by effervescent method. This may be due to the porous nature of tablet which makes it more friable. So maximum friability was 0.95% and the minimum friability 0.23% was observed for S5 and E6 respectively.

Content uniformity: The percentage of drug content was found to be between 96.977% and 101.55% for the formulations prepared by effervescent approach and the percentage of drug content was found to be between 97.53%-102.91% for the formulations prepared by sublimation approach. The average drug content of all the formulations is listed in table 3 and 4.

Wetting time: The graphical representations of wetting time of all the formulations prepared by effervescent method are depicted in figure 3.14.The average wetting time of all the formulation prepared by effervescent method are listed in table 3. The graphical representations of wetting time of all the formulations prepared by sublimation method are depicted in figure 3.15.The average wetting time of all the formulation prepared by sublimation method are listed in table 4. The tablets prepared by using effervescent method have shown wetting time between 16.58-45.25 seconds. Whereas tablets prepared by using sublimation method have shown wetting time between 3.97-20.44 seconds. Overall wetting time for formulations prepared by sublimation method was found to be the lowest (S7-3.97 seconds). This may be due to the porous nature of the tablet formulated by sublimation approach.

Disintegration time: The most important parameter that needs to be optimized in the development of orodispersible tablets is the disintegration time of the tablet. The graphical representations of disintegration time of all the formulations prepared by effervescent method are depicted in figure 3.16.The average disintegration time of all the formulation prepared by effervescent method are listed in table 3. The graphical representations of disintegration time of all the formulations prepared by sublimation method are depicted in figure 3.17.The average disintegration time of all the formulation prepared by sublimation method are listed in table 4. The tablets prepared by using effervescent method have shown disintegration time between 13-36 seconds. Whereas tablets prepared by using sublimation method have shown disintegration time between 7-39 seconds. Overall disintegration time for formulations prepared by sublimation method was found to be the lowest (S6-7 seconds) which meets

the objective of preparing ODT with disintegration time less than 10 seconds. This may be due to the porous nature of the tablet formulated by sublimation approach.

Effect of sodium bicarbonate in disintegration time: The result shows that disintegration time decreases with the increasing concentration of sodium bicarbonate. The formulation E13 having concentration of sodium bicarbonate 28.77% shows the disintegration time of 20 seconds.

Effect of camphor in disintegration time: The result of the formulations S1, S4 and S5 shows that the disintegration time decreases with increasing concentration of camphor. This may be due to the porous structure of the tablet which facilitates disintegration action of the superdisintegrant

Comparison of disintegration time of formulated batched with marketed product (MKT): Figure **Error! No text of specified style in document.**.1: Comparative study of disintegration time of the formulations prepared by effervescent method and sublimation method with marketed formulation. E11 (citric acid 16%, sodium bicarbonate 24% and crospovidone 4%), S6 (camphor 8%, crospovidone 4%). The result shows that the disintegration time of formulation prepared by effervescent method (13 secs) and sublimation method (7 secs) is least compared to marketed product (14 secs).

Dissolution test: *In vitro* dissolution test was performed as per USP. The *In vitro* dissolution test of all tablets formulated by direct compression and sublimation method were studied by using USP apparatus 2 at 37^0C $\pm 0.5^0$C at a rotation speed of 50 RPM. The dissolution medium consisted of 500ml of 0.1 N HCl. According to the USP, not less than 80 % Q of the labeled amount of ondansetron HCl is dissolved in 0.1 N HCl within 10 minutes. The percent of the drug released of formulation prepared by effervescent method was found to be in the range of 85.79%-100.26%. The average percentage released of all the formulation prepared by effervescent method is listed in table 3. The percent of the drug released of formulation prepared by sublimation method was found to be in the range of 85.49%-103.8%. The average drug releases of all the formulation prepared by sublimation method are listed in table 4.

Effect of sodium bicarbonate in dissolution rate: The percentage of drug release of formulation containing low concentration of sodium bicarbonate was found to be 88.24%. Considering formulations E2, E12 and E13 with concentration of crospovidone 3% and citric acid 13%, the maximum drug release was observed in E13 containing higher concentration of sodium bicarbonate (28.77%). This shows that with the increase in concentration of sodium bicarbonate the drug release was also increase d. It may be due effervescent property of sodium bicarbonate resulting in faster disintegration of tablet

Effect of camphor in dissolution rate: The percentage of drug release of formulation containing low concentrations of camphor was found to be 85.49%. Considering formulations S1, S4 and S5 with concentration of crospovidone 3%, the maximum drug release was observed in S5 containing higher concentration of camphor (17.65%). This shows that with increase in concentration of camphor the drug release was also increased. It could be due to the porous structure in the tablets which facilitates the wicking action of crospovidone.

Comparison between formulation methods: The disintegration time and wetting time of formulations prepared by sublimation method and effervescent method at fixed concentration of crospovidone (3% and 4%) were compared. In both the cases formulations prepared by sublimation method (S4, S5 at CP 3% and S6, S7 at CP 4%) showed minimum disintegration time and wetting time than the formulations prepared by effervescent method at same concentration of CP. The friability of the formulations prepared by effervescent was found to be in the range of 0.23%- 0.58% and that of formulations prepared by sublimation method was found to be within range of 0.64%-0.95%. Among the two formulations, the tablets prepared by sublimation method were more friable suggesting difficulty in handling and packaging. The tablets prepared by effervescent method have yet another advantage of masking the taste of bitter drug. Due to evolution of carbon dioxide the bittertaste of drug is also masked and pleasant mouthfeel is felt [24]. Ondansetron hydrochloride being a bitter drug, formulation by effervescent method would be appropriate. However, considering the objective of formulating ODT with least disintegration time, formulation with sublimation method seems to be more effective. Hence, sublimation method was found to be more effective than effervescent method.

CONCLUSIONS

Orodispersible tablets of ondansentron hydrochloride can be formulated using two different approaches: sublimation and effervescent method which could give desired DT of less than 15 seconds. Ondansetron hydrochloride prepared by sublimation method using camphor (6.34-

17.65%) and crospovidone (1.58-4.41%) and effervescent method incorporating crospovidone (1.31%-4.68%), citric acid (7.95%-18.04%) and sodium bicarbonate (5.22%-28.77%) formulated using factorial design could help us achieve this objective. Thus, such approaches could be effective in formulating orodispersible tablets of ondansetron hydrochloride beneficial for pediatrics, geriatrics and psychiatric patients and will also help to improve patient compliance.

Acknowledgements: The authors are thankful to Lomus Pharmaceuticals Pvt. Ltd. for providing Metformin Hydrochloride and various grades of HPMC as a gift samples and National Model College for Advance Learning for providing necessary facilities to carry out this work.

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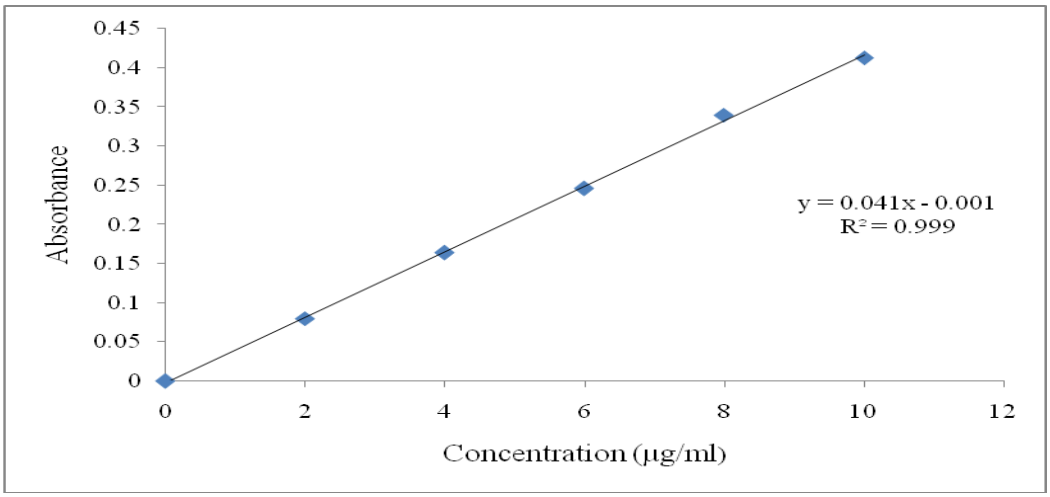

Figure 1: Calibration curve of ondansetron HCl reference standard in 0.1 N HCl

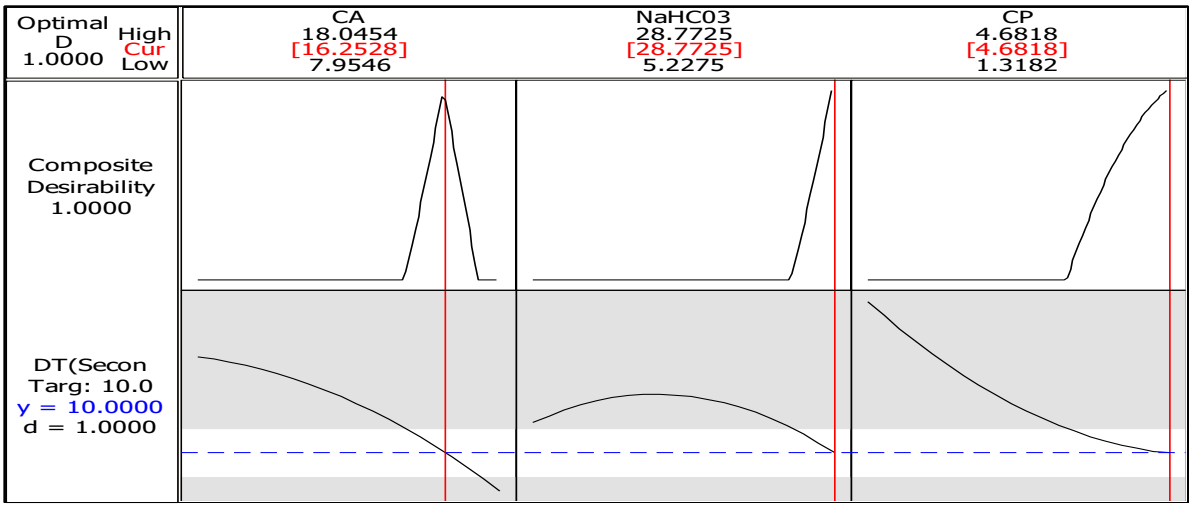

Figure 2: Optimization of composite responses of three variables

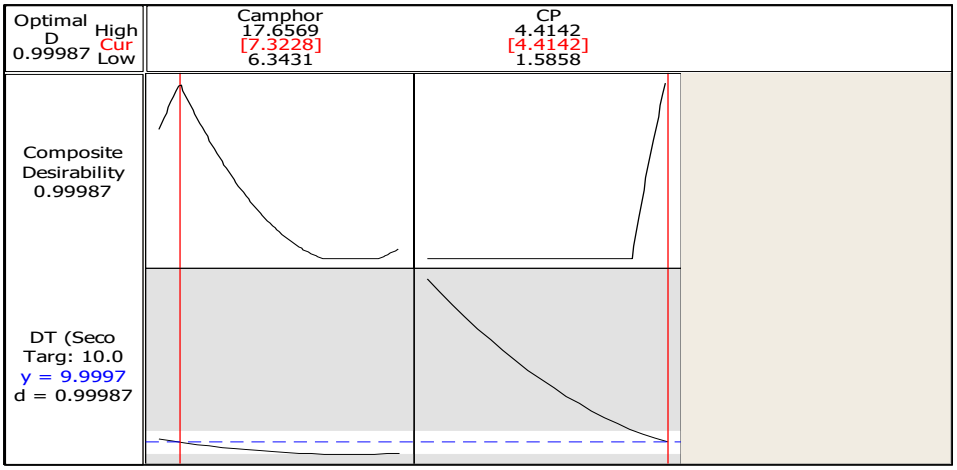

Figure 3: Optimization of composite responses of two variables

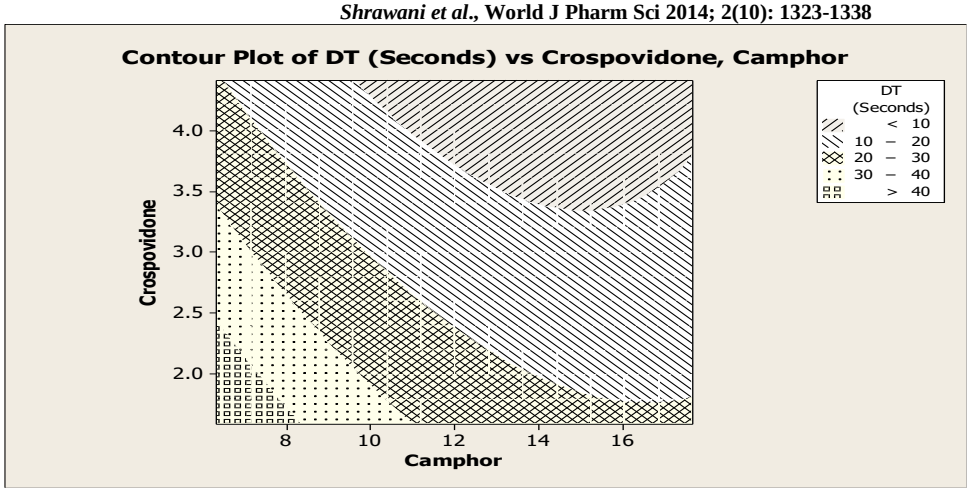

Figure 4: Contour plot of disintegration (seconds) vs crospovidone, camphor

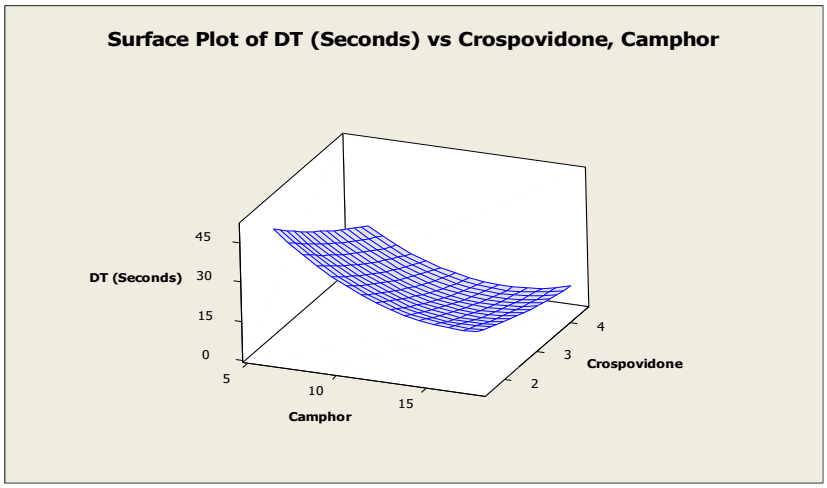

Figure 5: Surface plot of disintegration (seconds) vs crospovidone, camphor

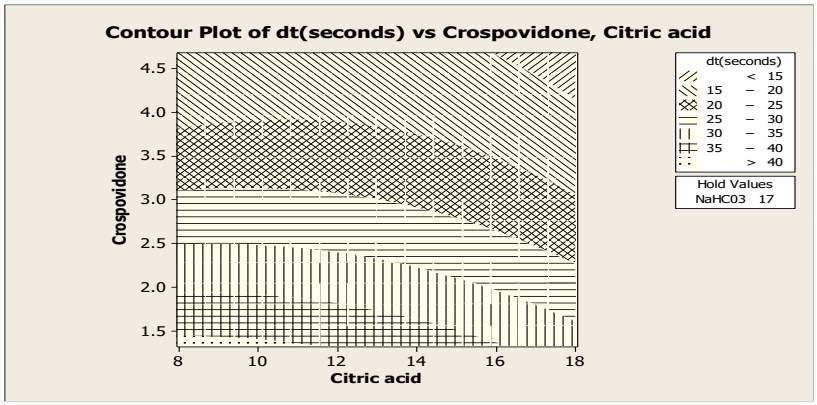

Figure 2: Contour plot of disintegration (seconds) vs crospovidone, citric acid

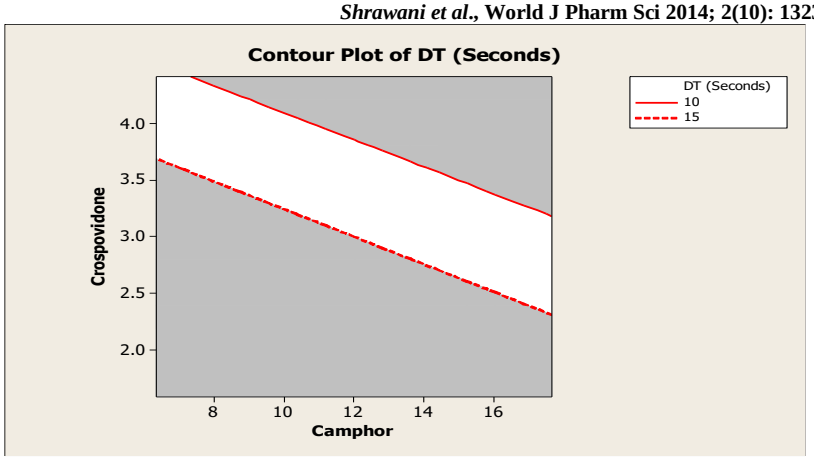

Figure 7: Overlaid contour plot of disintegration (seconds)

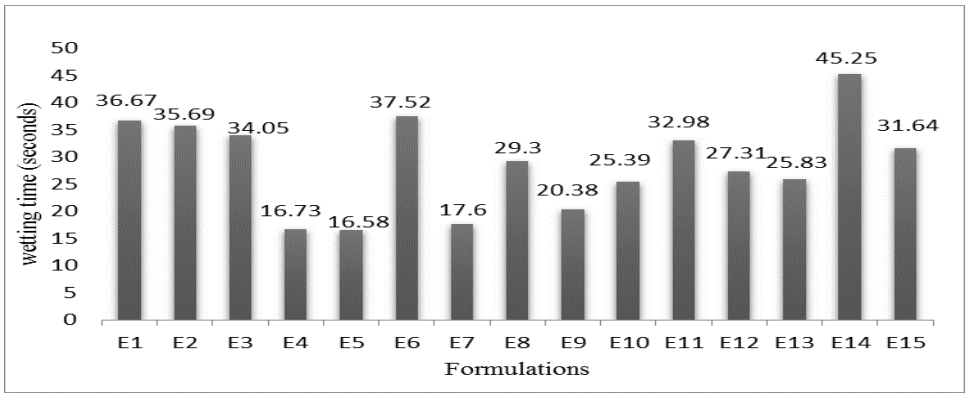

Figure 8: Wetting time of formulations prepared by effervescent method

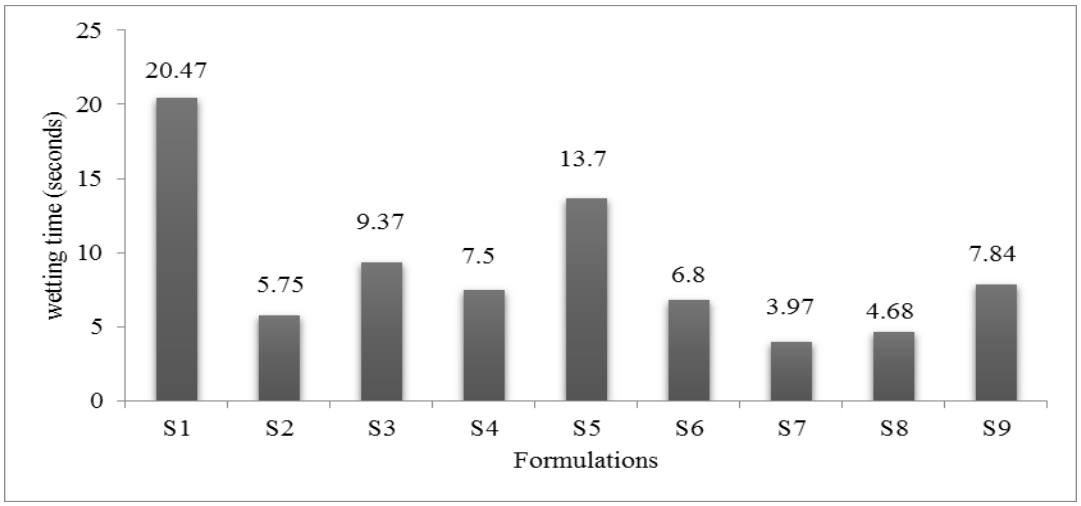

Figure 9: Wetting time of formulations prepared by sublimation method

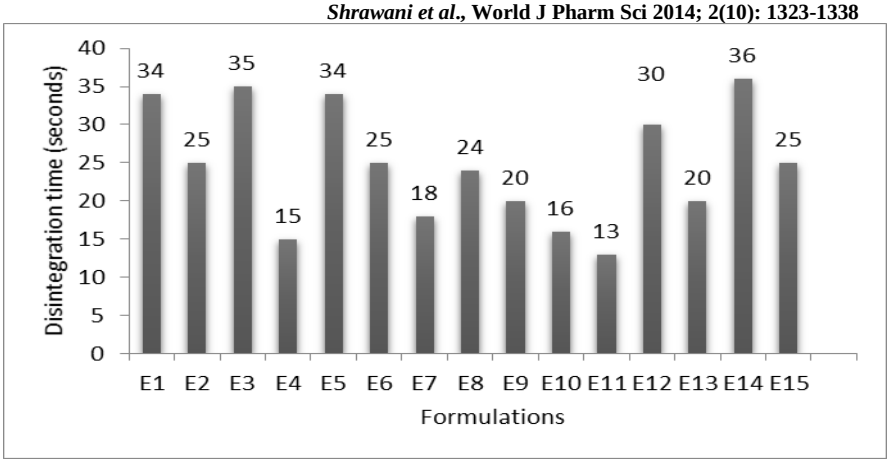

Figure 10: Disintegration time of formulations prepared by effervescent method

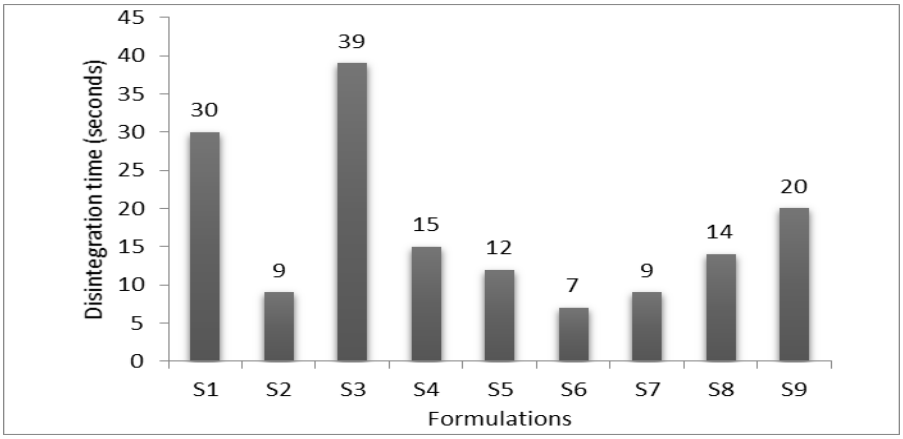

Figure 11: Disintegration time of formulations prepared by sublimation method

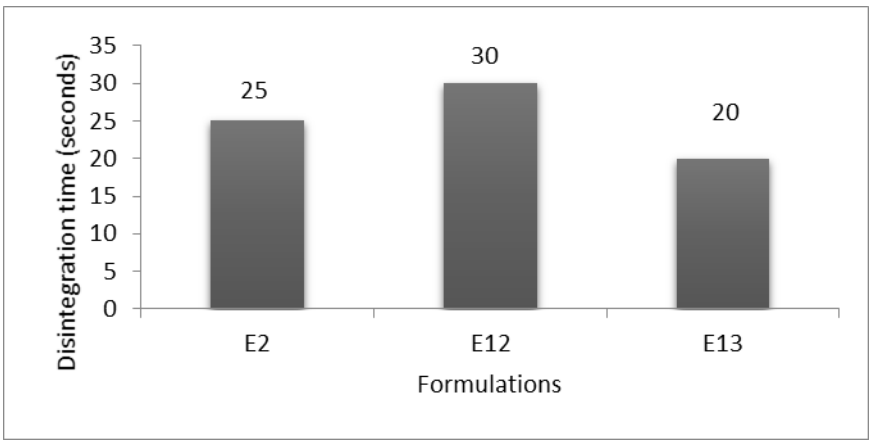

Figure 12:Comparative study of disintegration time of formulations prepared by effervescent method using different concentrations of sodium bicarbonate and 3% crospovidone and 13% citric acid.E2 (sodium bicarbonate 17%), E12 (sodium bicarbonate 5.22%) and E13 (sodium bicarbonate 28.77%)

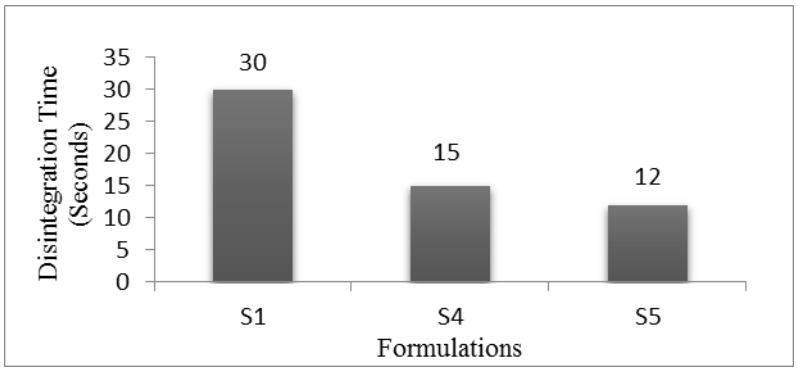

Figure 13: Comparative study of disintegration time of formulations prepared by sublimation method using different concentrations of camphor and crospovidone (2%).S1 (camphor 6.34%), S4 (camphor 12%) and S5 (camphor 17.65%)

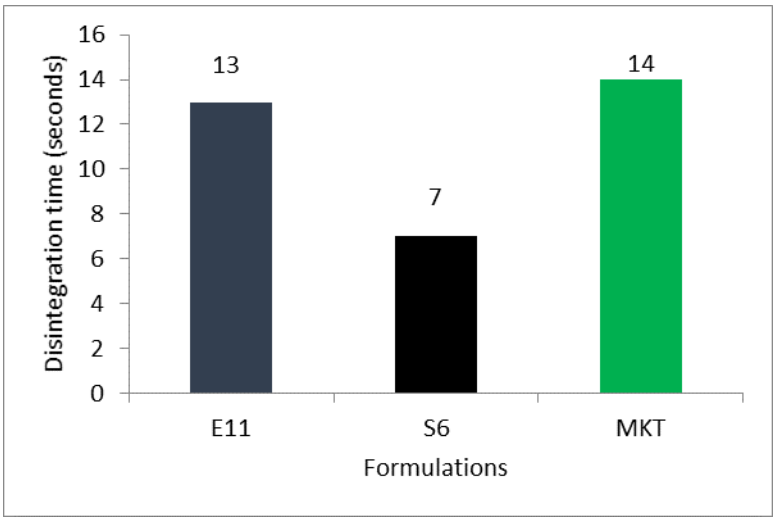

Figure 14: Comparative study of disintegration time of the formulations prepared by effervescent method and sublimation method with marketed formulation. E11 (citric acid 16%, sodium bicarbonate 24% and crospovidone 4%), S6 (camphor 8%, crospovidone 4%)

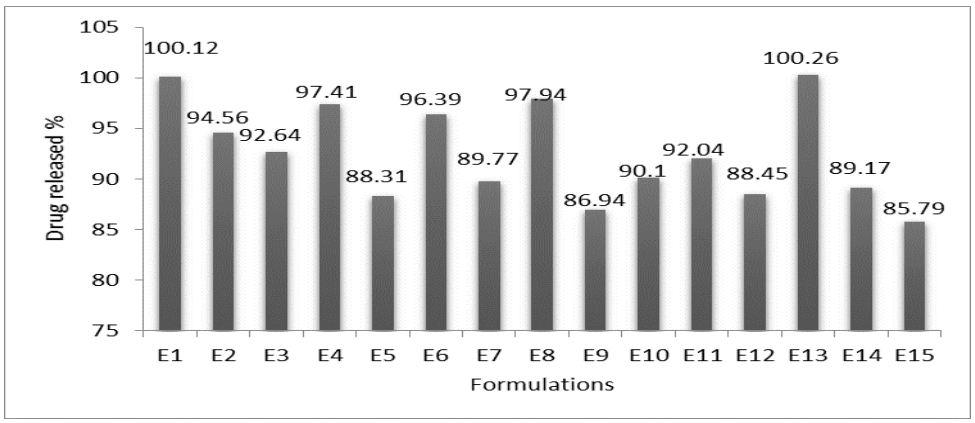

Figure 15: Comparative study of drug release of formulations prepared by effervescent method

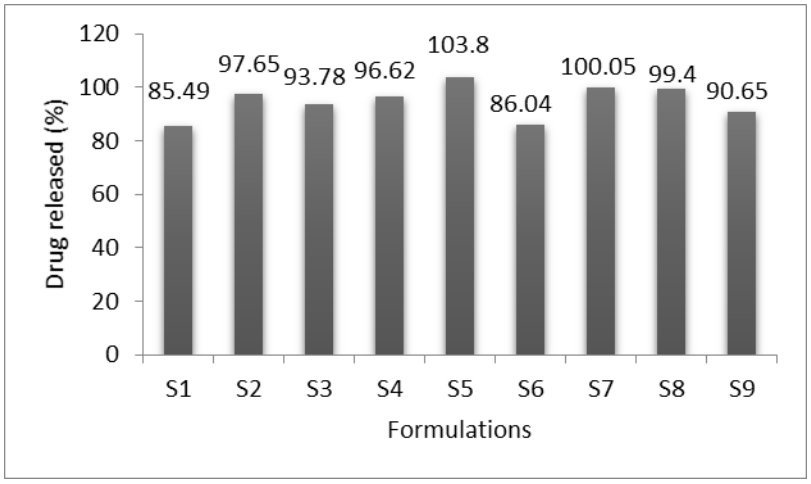

Figure 16: Comparative study of drug release of formulations prepared by sublimation method

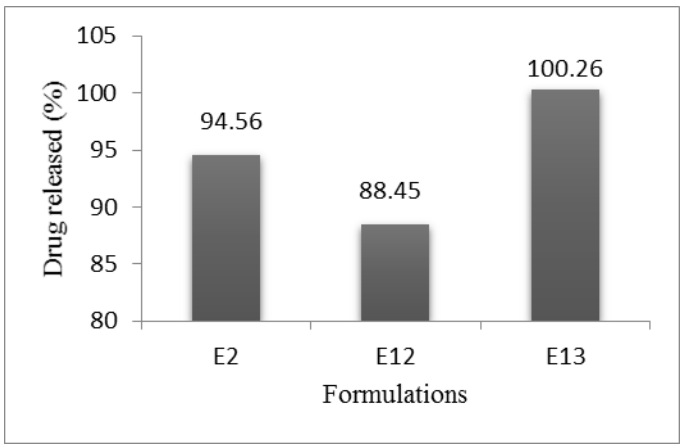

Figure 17: Comparative study of dissolution rate of formulations prepared by effervescent method using different concentrations of sodium bicarbonate and 3% crospovidone and 13% citric acid.E2 (sodium bicarbonate 17%), E12 (sodium bicarbonate 5.22%) and E13 (sodium bicarbonate 28.77%).

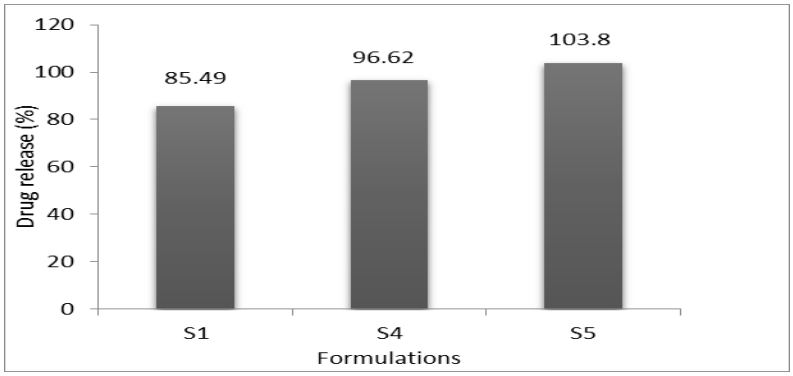

Figure 18: Comparative study of drug release of formulations prepared by sublimation method using different concentration of camphor and and 2% crospovidone. S1 (camphor 6.34%), S4 (camphor 12%) and S5 (camphor 17.65%)

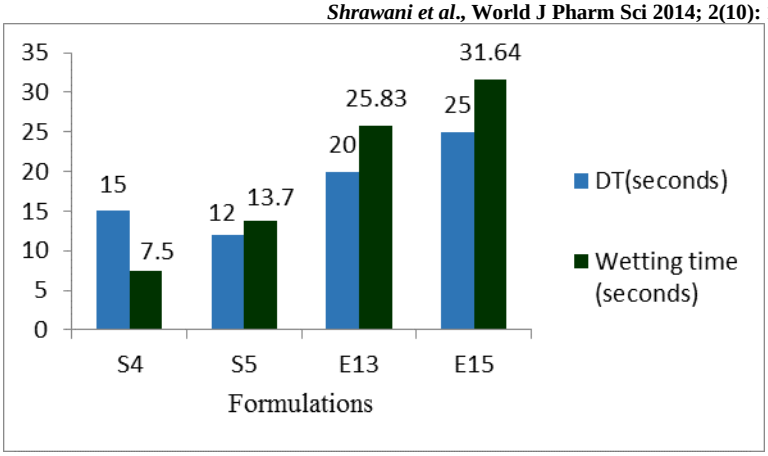

Figure 19: Comparative study of disintegration time and wetting time of formulations prepared by sublimation method and effervescent method using crospovidone 3%. S4 (camphor 12%), S5 (camphor 17.65%), E13 (citrc acid 13% and sodium bicarbonate 28.77%), E15 (citric acid 18.04% and sodium bicarbonate 17%)

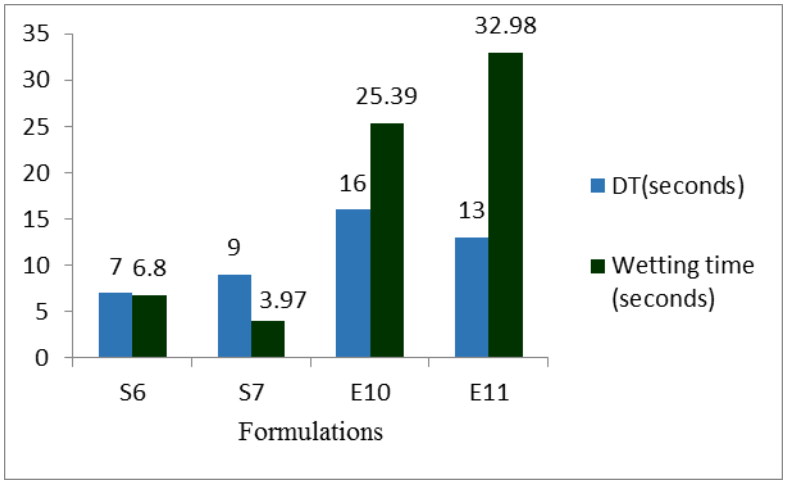

Figure 20: Comparative study of disintegration time and wetting time of formulations prepared by sublimation method and effervescent method using crospovidone 4%.S6 (camphor 8%), S7 (camphor 16%), E10 (citric acid 10% and sodium bicarbonate 10%), E11 (citric acid 16% and sodium bicarbonate 24%)

Ingredient/Batche	E1	E2	E3	E4	E5	E6	E7	E8	E9
Ondansetron	8mg	8mg	8mg	8mg	8mg	8mg	8mg	8mg	8mg
MCC	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)
Mannitol	49(24.5%)	39(19.5%)	61(30.5%)	45(22.5%)	33(16.5%)	49.1(24.55%)	29(14.5%)	21(10.5%)	35.64(17.82%)
Citric acid	32(16%)	26(13%)	20(10%)	32(16%)	20(10%)	15.9(7.95%)	20(10%)	32(16%)	26(13%)
Sodium	20(10%)	34(17%)	20(10%)	20(10%)	48(24%)	34(17%)	48(24%)	48(24%)	34(17%)
Crospovidone	4(2%)	6(3%)	4(2%)	8(4%)	4(2%)	6(3%)	8(4%)	4(2%)	9.3(4.68%)
MST	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)
Talc	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)
Saccharin	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)
Total (mg)	200	200	200	200	200	200	200	200	200

Ingredient/batches	E10	E11	E12	E13	E14	E15
Ondansetron	8mg	8mg	8mg	8mg	8mg	8mg
MCC	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)
Mannitol	57(28.5%)	17(8.5%)	62.545(31.2725%)	15.46(7.73%)	42.363(21.1817%)	28.909(14.4546%
Citric acid	20(10%)	32(16%)	26(13%)	26(13%)	26(13%)	36.09(18.0454%)
Sodium bicarbonate	20(10%)	48(24%)	10.455(5.2275%)	57.54(28.77%)	34(17%)	34(17%)
Crospovidone	8(4%)	8(4%)	6(3%)	6(3%)	2.636(1.31821%)	6(3%)
Magnesium stearate	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)
Talc	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)
Saccharin	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)
Total (mg)	200	200	200	200	200	200

Table 2: Composition of formulations prepared by sublimation approach

Ingredient/batches	S1	S2	S3	S4	S5	S6	S7	S8	S9
Ondansetron	8mg	8mg	8mg	8mg	8mg	8mg	8mg	8mg	8mg
MCC	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)	80(40%)
Mannitol	86.3(43.15%)	72.16(36.08%)	77.8(38.91%)	75(37.5%)	63.7(31.85%)	81(40.5%0	65(32.5%)	69(34.5%)	85(42.5)
Camphor	1.268(6.3431%)	24(12%)	24(12%)	24(12%)	35.3(17.6569%)	16(8%)	32(16%)	32(16%)	16(8%)
Crospovidone	6(3%)	8.8(4.41421%)	3.17(1.58579%)	6(3%)	6(3%)	8(4%)	8(4%)	4(2%)	4(2%)
MST	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)	2(1%)
Talc	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)	4(2%)
Saccharin	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)
Total (mg)	200	200	200	200	200	200	200	200	200

Table 3: Physicochemical parameter analysis of formulations prepared by effervescent approach

Batch	Wt.Variation n=20	Hardness(kg/cm^2) n=6	Thickness(mm) n=10	Friability (%) n=20	Disintegration time(seconds)	Dissolution (%)	Wetting time (seconds) n=6	Content Uniformity (%)
E1	0.200±0.002	2.1±0.2236	3.76±0.0576	0.30	34	100.125±3.00	36.67±3.713428	96.977±2.1553
E2	0.201±0.003	2.3±0.27386	3.64±0.016	0.28	25	89.391±1.341	35.69±3.34345	98.233±1.420
E3	0.201±0.001	2.8±0.27386	3.76±0.05464	0.34	35	92.64±0.7412	34.05±2.548874	101.35±2.058907
E4	0.201±0.001	2.8±0.27386	3.90±0.0126	0.27	15	97.416±1.453	16.73±3.341	100.4±2.130634
E5	0.201±0.002	2.7±0.27386	3.92±0.0617	0.26	34	88.318±2.248	16.58±2.5275	98.53±1.708186
E6	0.199±0.003	3.7±0.27386	3.95±0.0453	0.23	25	96.399±0.891	37.52±5.602808	98.51±1.096099
E7	0.204±0.001	2.7±0.27386	3.79±0.0491	0.34	18	89.776±2.372	17.60±3.02649	101.55±0.826821

E8	0.203±0.001	3.8±0.27386	3.65±0.0655	0.48	24	97.945±1.995	29.30±2.193363	98.71±0.547844
E9	0.204±0.002	2.7±0.27386	3.89±0.0433	0.37	20	86.942±1.453	20.38±2.834424	99.07±0.735686
E10	0.202±0.001	2.3±0.27386	3.70±0.0248	0.53	16	90.106±1.517	25.39±4.368768	99.48±0.848842
E11	0.203±0.002	2.7±0.27386	3.82±0.0371	0.25	13	92.04±1.8902	32.98±2.916816	101.90±1.661365
E12	0.201±0.002	3.8±0.27386	3.75±0.0553	0.46	24	88.245±1.170	27.31±6.199371	98.55±1.041601
E13	0.202±0.002	3.7±0.27386	3.76±0.0628	0.58	20	89.798±1.824	25.83±1.794496	98.32±1.958069
E14	0.201±0.002	2.6±0.27386	3.74±0.0441	0.39	36	85.798±0.866	45.25±1.743257	98.81±0.580718
E15	0.200±0.002	3.6±0.27386	3.66±0.0484	0.46	25	98.498±1.110	31.645±2.2226	101.46±0.931146

Table 4: Physicochemical parameter analysis of formulations prepared by sublimation approach

Batch	**Weight Variation n=20**	**Hardness (kg/cm^2) n=6**	**Thickness (mm) n=10**	**Friability (%) n=20**	**Disintegration time(seconds)**	**Dissolution (%)**	**Wetting time (seconds)**	**Content uniformity (%)**
S1	0.186±0.00363	3.7±0.273861	3.83±0.022361	0.64	30	98.49±1.110683	20.44±3.5254	101.46±0.931
S2	0.182±0.00313	2.3±0.273861	3.96±0.018028	0.81	9	89.80±2.049458	5.75±1.52340	98.73±0.5565
S3	0.179±0.00229	2.7±0.273861	3.81±0.050498	0.78	39	89.21±1.986749	9.37±0.98796	99.21±0.2914
S4	0.180±0.00383	2.7±0.570088	4.04±0.033166	0.75	15	87.77±1.4466	7.55±0.69819	102.91±2.249
S5	0.182±0.00313	3.8±0.273861	3.85±0.041062	0.95	12	103.80±3.2989	13.76±2.0143	102.28±1.708
S6	0.179±0.00286	2.7±0.570088	4.05±0.01236	0.69	7	94.83±4.468275	6.81±1.10391	101.78±1.410
S7	0.178±0.00365	3.5±0.353553	3.83±0.040654	0.86	9	88.10±1.514737	3.97±0.82990	99.08±0.4150
S8	0.180±0.00356	2.7±0.273861	4.03±0.040242	0.83	14	89.54±13.23136	4.68±1.13353	97.53±1.7024
S9	0.181±0.00361	2.6±0.223607	4.05±0.031623	0.72	20	90.65±2.797597	7.84±0.96760	100.95±0.433