



Research articles

Optimized fast disintegrating tablets, boosted oseltamivir phosphate orally fast disintegrating tabletsPeeush Singhal^{2*}, Piyush chamola¹, Vijay Jyoti Kumar¹, Sarvesh Kumar³, Abhiram Rout³¹H.N.B. Garhwal (A Central University) Srinagar, Uttarakhand, India²Gurukul Kangri (Deemed to be University), Haridwar, Uttarakhand, India³Krishna Pharmacy College, Noorpur Road, Bijnor, Uttarpradesh, India**ABSTRACT**

Background Around 33% of the populace (fundamentally pediatric and geriatric) has gulping hardships, bringing about helpless consistence with oral tablet drug treatment which prompts decreased in general treatment viability. For this explanation, tablets that can quickly break down or deteriorate in the oral cavity have drawn in a lot of consideration. Objective research was designed to develop and evaluate boosted orally fast disintegrating tablets (OFDT) for oro-buccal drug delivery of oseltamivir phosphate. **Methods** In the present study six formulations of mouth dissolving tablet of oseltamivir were prepared by direct compression method using SSG as a super disintegrating agent with lactose, talcum, mannitol, SLS and starch. The prepared tablets were then subjected to various evaluation parameters. Results every one of the outcomes was observed to be inside satisfactory reaches. The formulation F6 manufacturing utilizing SSG 50mg and SLS 10mg showed the higher medication content (98%), while the formulation F2 showed the least medication content (92%). It was seen that with the increment in SSG concentration, the medication content was additionally increased. SEM concentrate on showed request of expanding unpleasantness of tablet surface is F1<F2<F3<F4<F5<F6. The expanding unpleasantness may be answerable for higher % of medication release. Formulation F1 showed the most elevated medication discharge (97.735%), while the formulation F5 showed the least medication discharge (56.24%). Finally, it was inferred that SSG, SLS, D-mannitol, starch, lactose, and talcum powder can be effectively utilized in the formulation of Oseltamivir phosphate mouth dissolving tablets. **Conclusion:** From the above work it was presumed that the formulation of the Oseltamivir Phosphate was observed to be more achievable than the regular one.

Keywords: Oseltamivir Phosphate, Mouth Dissolving Tablet, Scanning Electron Microscopy, Super Disintegrating Agent.

Received – 09/07/2021, Reviewed - 14/08/2021, Revised/ Accepted- 04/11/2021

Correspondence: Dr. Peeush Singhal* ✉ peeushpharma@gmail.com

Gurukul Kangri (Deemed to be University), Haridwar, Uttarakhand, India

INTRODUCTION

The traditional dosage forms tablet and capsule have wide acknowledgment up to 50-60% of absolute dose forms. Tablet is still most well-known regular dosage forms existing today due to simplicity of self-organization, minimized in nature, simple to fabricate and it tends to be conveyed in precise portion. ^[1]

One significant downside of solid dosage forms is the trouble in gulping (dysphasia) or biting in certain patients especially pediatric and geriatric patients. The issue of gulping is normal marvel in geriatric patient because of dread of gagging, hand quakes, dysphasia and in youthful people because of immature muscular and sensory systems and in schizophrenic patients which prompts helpless patient consistence.

Troubles in gulping of tablet and capsule are additionally happens when water isn't available, in loose bowels, coughing during

the normal chilly, hypersensitive condition and bronchial disease. Roughly 33% of the populace (fundamentally pediatric and geriatric) has gulping hardships, bringing about helpless consistence with oral tablet drug treatment which prompts decreased by and large treatment adequacy.

For these explanations, tablets that can quickly break down or crumble in the oral cavity have drawn in a lot of consideration. ^[2]

United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) as “a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue”. ^[3]

Quick dissolving tablets are otherwise called mouth-dissolving tablets, soften in mouth tablets, Or dispersible tablets, rapimelts, permeable tablets, speedy dissolving tablet.

MATERIAL AND METHOD

Oseltamivir and SSG were purchased from jubilent generic Ltd. Noida. SLS, lactose, talcum, mannitol and starch were obtained from Central Drug House, Mumbai. All other chemicals used were of analytical grade.

Method for Preparation

Mouth dissolving tablets were prepared by direct compression method. Accurately weighed drug and excipients in different ratios were mixed together and then placed in single tablet punching machine. Total 6 formulations figure.1, figure. 2, figure. 3, figure. 4, figure. 5 and figure. 6 were prepared. The composition of different mouth dissolving tablet of Oseltamivir phosphate is given in table 1 and prepared MDTs are shown in figure 1.

Table 1: Composition of MDTs of oseltamivir

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Lactose	90	90	90	90	90	90
Oseltamivir	75	75	75	75	75	75
SSG	10	20	30	40	45	50
SLS	10	10	10	10	5	10
Talcum	2	2	2	2	2	2
D-mannitol	2	2	2	2	2	2
Starch	50	40	30	20	20	10

Figure 1: Photographs of MDTs of oseltamivir



Figure 2



Figure 3



Figure 4



Figure 5



Figure 6



CHARACTERIZATION AND EVALUATION

FTIR Analysis

To examine excipients similarity and recognizable proof of medication, FTIR Analysis of Oseltamivir, Lactose, SSG, SLS, Talcum, Mannitol, and Starch was performed by Potassium Bromide (KBr) disc method. Both sample 1mh and KBr300mg were taken in mortar and pulverized, then, at that point, were spreaded consistently in a reasonable die the bucket packed under vacuum at a tension of around 800 MPa in the KBr press, resultant circle were then mounted in an appropriate holder in the spectrophotometer (Perkin Elmer Spectrum variant 10.03.05 model L1600300, Egilent) and the spectra between 4000cm⁻¹ to 400cm⁻¹ were recorded. The FTIR range of the secured drug sample was contrasted and the standard range of the unadulterated medication for distinguishing proof.

Drug content

The drug content in oseltamivir mouth dissolving tablet was determined by taking accurately weighed tablet in a beaker, left for 2h with continuous stirring by magnetic stirrer using Teflon coated magnetic bead. The temperature was maintained at 37°C. At the end of 2nd h, it was filtered, and diluted suitably using water then analyzed by spectrophotometrically at 221nm (ESICO International). The drug contents were calculated using formula:

$$\text{Drug content} = \frac{\text{Concentration of drug in final formulation}}{\text{concentration of drug initially loaded to tablets}} \times 100$$

Micromeritics evaluation

The formulations were subjected for Micromeritics evaluations.

- Particle size and surface morphology was determined by optical microscopy and Scanning electron microscopy (EVO 40 EP, Zeiss, USA).
- Angle of repose the 5 g of powder mixture was poured into glass funnel; the lower tip of glass funnel was 5 cm height from the ground. The height (h) and radius (r) of pile were measured, and

then calculated by equation:

$$\theta = \tan^{-1} \frac{h}{r}$$

Where θ = angle of repose ($^{\circ}$), h = height (cm), r = radius (cm)

- Bulk density 20 g of powder mixture was weighted accurately, gently poured into 100 ml glass cylinder without compacting. The volume of powder mixture was recorded, and then calculated by equation:

$$\text{Bulk density} = \frac{m}{V_0}$$

Where m = mass (g), V_0 = unsettled apparent volume (cm^3)

- Tapped density 20 g of powder mixture was weighted accurately, poured into 100 ml glass cylinder. It was tapped using tapped density tester (Erweka D-63150, Germany) for 1,250 strokes. The volume of tapped powder mixture was recorded, and then calculated by equation:

$$\text{tapped density} = \frac{m}{V_f}$$

Where m = Weight of powder and v_f = Volume of packing after tapings.

- Carr's compressibility index (%) It was calculated from the bulk density and the tapped density data using the following formula:

$$\text{C.I. (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}}$$

- Hausner's ratio Hausner's ratio was calculated by equation

$$\text{H.R.} = \frac{\text{Tapped density (pt)}}{\text{Bulk density (pb)}}$$

Evaluation parameters of mouth dissolving tablets

Weight variation

Twenty tablets were weighed individually. Each tablet weight was recorded. Results were reported as mean standard deviation in milligrams (mg) units. The weight variation was calculated as per the limits of IP. (Table 2)

Table 2: Weight variation as per I.P average

Weight of tablet	% Deviation
80mg or less	$\pm 10\%$
More than 80mg but less than 250mg	$\pm 7.5\%$
250mg or more	$\pm 5\%$

Friability

Ten tablets were accurately weighed together, and friability was tested using a friability tester. After 4 min of rotation at 25 rpm, any loose dust from the tablets was removed before accurately weighing again. The friability was calculated by equation:

$$\text{friability} = \frac{W_{\text{before}} - W_{\text{after}}}{W_{\text{before}}} \times 100$$

Where W_{before} = weight of tablets before test (g),

W_{after} = weight of tablets after test (g)

Thickness

Ten tablets were separately estimated utilizing vernier

caliper at various marks of the tablets and the average was determined.

Hardness

The restriction of hardness for the FDT is generally kept in a lower reach to work with early deterioration in the mouth. The hardness of the tablet might be estimated utilizing ordinary hardness analyzers (Monsanto tablet hardness analyzer). Ten tablets were estimated utilizing a hardness analyzer. It is expressed in kg or pound

Disintegration time

Six tablets were tested by a disintegration tester (MAC Tablet Disintegration Test Machine USP/IP/BP STD.) Following the United State Pharmacopoeia method and water was used as the disintegration medium at 37°C . DT of each tablet was recorded in minutes.

Moisture Uptake Studies

It was conducted to evaluate the security of the formulation. Ten tablets from every formulation were kept in a desiccator over calcium chloride at 37°C for 24 h. The tablets were then weighed and presented to 75% relative mugginess at room temperature for quite 2 weeks. Required moistness was accomplished by keeping immersed sodium chloride arrangement at the lower part of the desiccators for 3 days. One tablet as control (without SSG) was kept to evaluate the dampness take-up due to other excipients. Tablets were weighed and the rate expansion in recorded.

RESULTS

In the current review mouth dissolving tablets of oseltamivir was effectively ready by direct pressure strategy utilizing SSG as a super crumbling agent. The manufactured tablets were then exposed to different assessment boundaries, for example, Drug content examination, Micromeritics assessment, FTIR, Scanning Electron Microscopy and In-vitro dissolution study and so forth.

FTIR analysis

The compatibility studies of drug and excipients were performed by FTIR analysis (Perkin Elmer Spectrum version 10.03.05 model L1600300, Egilent).

Infrared (IR) spectrum of Oseltamivir phosphate showed characteristics absorption peaks at 721.92 cm^{-1} , indicating NH_2 and N-H wagging (shifts on H-bonding). The absorption peaks at 2724 cm^{-1} , 1455 cm^{-1} were due to C-H aldehyde and CH_2 and CH_3 deformation. (Figure 2)

Drug polymers interaction

FTIR spectrums of drug and polymers interaction are as follows
As the peak observed in physical mixture of drug and polymers have no interference, therefore no chemical interaction was observed between them. From FTIR study it was concluded that the physical mixture of drug and all polymers are compatible with each other's (Figure 3).

Figure 2: FTIR spectrum of procured sample of Oseltamivir

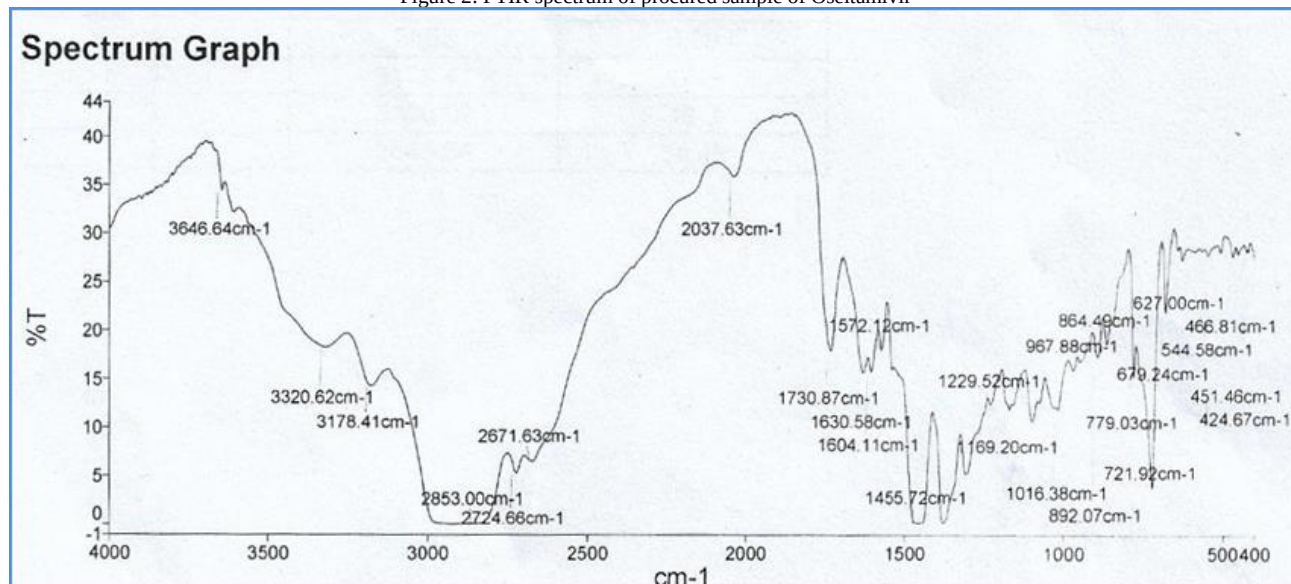
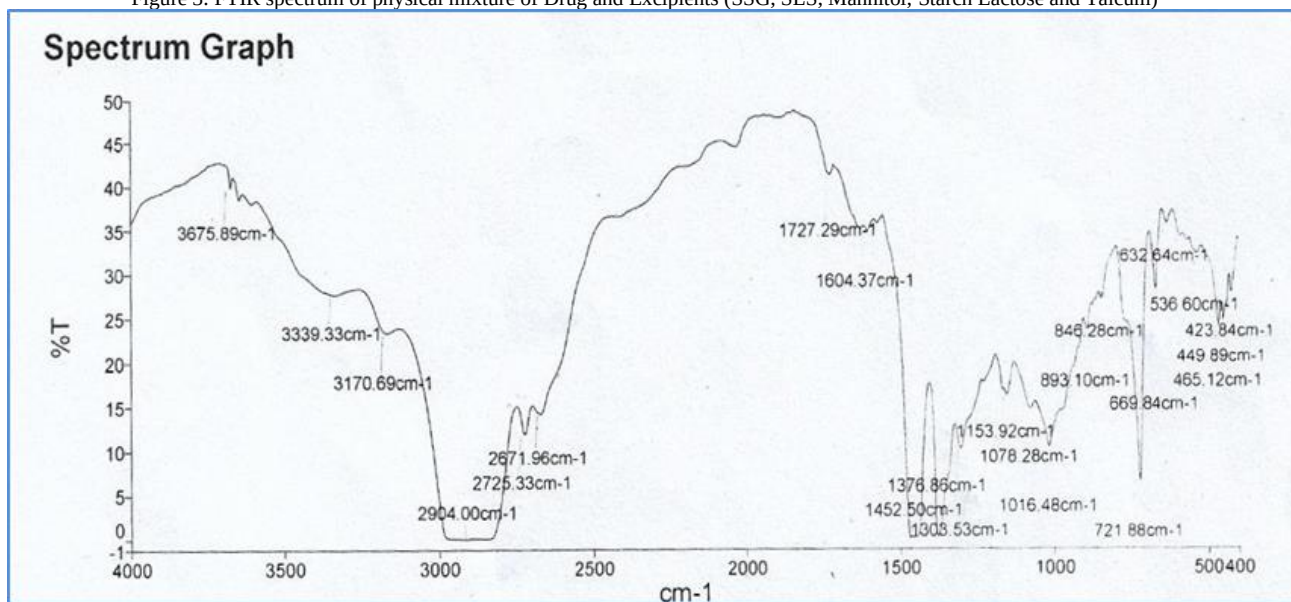


Figure 3: FTIR spectrum of physical mixture of Drug and Excipients (SSG, SLS, Mannitol, Starch Lactose and Talcum)

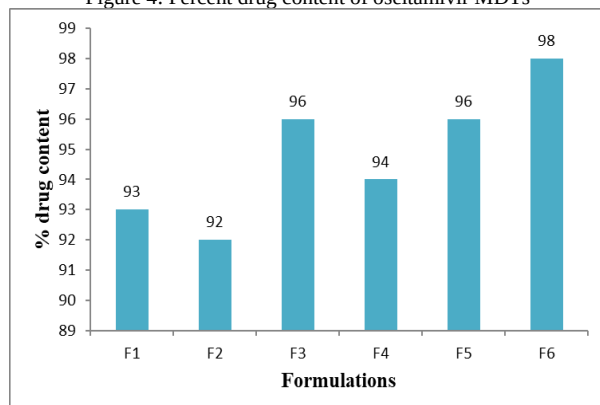


Characterization and evaluation of the MDTs

Drug content analysis

Drug content analysis was done for all the formulations of oseltamivir using the phosphate buffer pH 6.8 as the medium and the result are shown graphically in Figure4.

Figure 4: Percent drug content of oseltamivir MDTs



The formulation F6 prepared using SSG 50mg and SLS 10mg showed the higher drug content (98%), while the formulation

F2 showed the least drug content (92%). It was observed that with the increase in SSG concentration, the drug content was also increased. Drug content was found to be uniform among the all formulation and ranged from 92% to 98%.

Micromeritics evaluations

The prepared mouth dissolving tablets were subjected to various Micromeritics evaluation parameters such as particle size, bulk density, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose etc. [17]

Bulk density, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose were calculated for all the formulations for evaluating of the flow properties of formulated oseltamivir MDTs, the results are compiled in Table 3.

The evaluations parameters such as: Friability, Hardness, Weight

variation, Tablet thickness and Disintegration times are compiled in table 4.

Table 3: Micromeritics Evaluation of Oseltamivir MDTs.

S. No.	Bulk density	Tapped density	Carrs index	Hausner Ratio	Angle of repose	Flow
F1	0.473 ± 0.016	0.055 ± 0.090	15.157	1.178	32.21	Good
F2	0.495 ± 0.054	0.623 ± 0.024	20.510	1.258	33.02	Fair
F3	0.482 ± 0.029	0.543 ± 0.024	11.167	1.125	32.61	Good
F4	0.423 ± 0.026	0.532 ± 0.025	20.433	1.256	37.95	Fair
F5	0.523 ± 0.012	0.662 ± 0.023	21.011	1.266	41.98	Passable
F6	0.504 ± 0.055	0.557 ± 0.091	9.523	1.105	28.81	Excellent

*Data expressed as mean values and standard deviation ($\pm$ S.D); n=3

Table 4: Evaluation of Oseltamivir phosphate MDTs.

Formulation	Hardness (kg/cm ²)	Friability (%)	Weight variation (mg)	Thickness (mm)	Disintegration time (sec)
F1	3.2±0.11	0.33±0.05	236±0.08	2.21±0.12	78±0.013
F2	3.3±0.17	0.39±0.01	237±0.08	2.29±0.22	62±0.021
F3	3.1±0.10	0.32±0.02	236±0.19	2.22±0.09	57±0.066
F4	3.0±0.11	0.36±0.7	240±0.23	2.21±0.55	48±0.051
F5	2.9±0.19	0.38±0.09	238±0.12	2.28±0.71	42±0.011
F6	2.8±0.12	0.42±0.04	235±0.11	2.27±0.33	38±0.080

All the formulated (F1 to F6) tablets breezed through weight variety assessment as the % weight variety was inside the IP furthest reaches of $\pm 7.5\%$ of the weight. The normal thickness of the all formulation was observed to be 2.24 mm and inside the restriction of standard Pharmacopeia. [18].

The hardness of the tablet was observed to be 2.8 to 3.3 kg/cm². The greatest friability of the formulation was observed to be 0.4%. The base friability of the formulation was observed to be 0.3%. The % friability was under 1% in every one of the formulations guaranteeing that the tablets were mechanically stable. The tablets showed breaking down time not exactly explicit cutoff (3 min) for mouth dissolving tablets. [19].

As per the observations from FTIR spectra no major changes or the shifting in the peaks of drug were observed which indicates that there happens no chemical interaction between the drug and polymers physical mixtures. It was presumed that the medication is available in free form in all the formulation independent of the variety in the composition. [20].

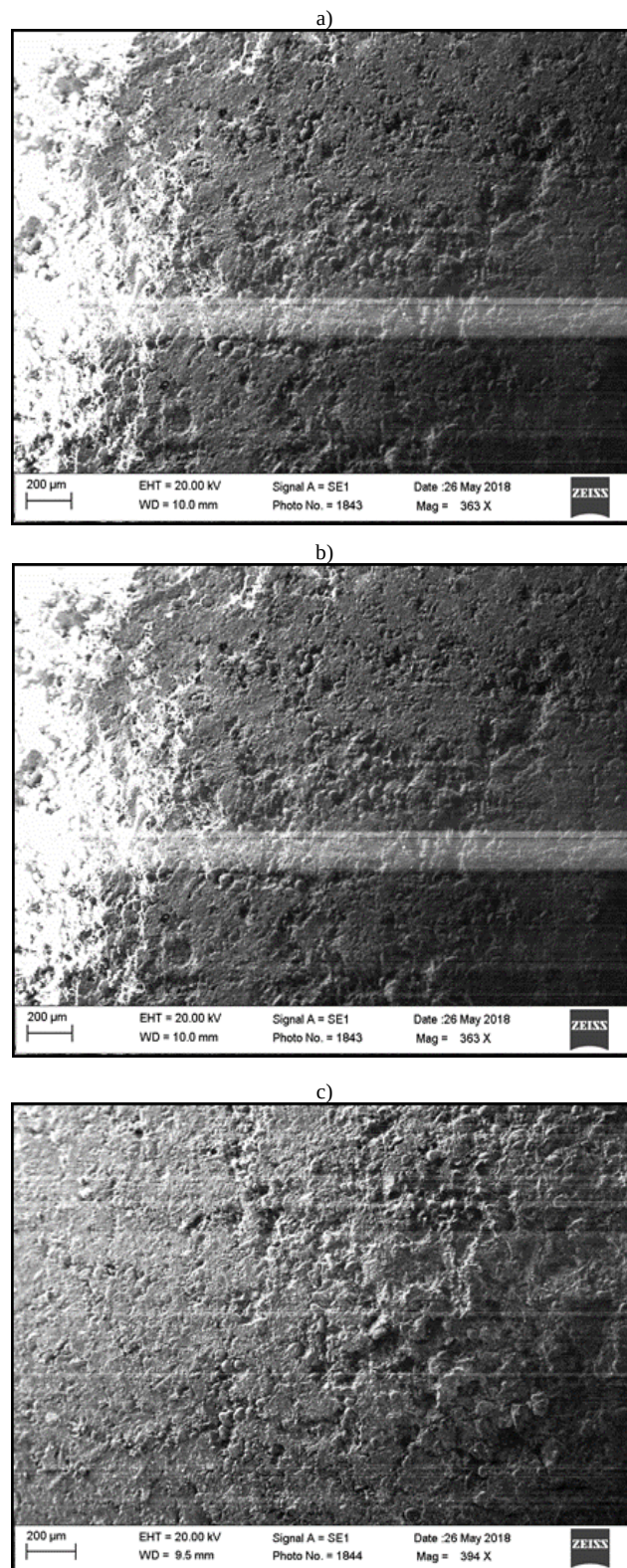
Scanning electron microscopy

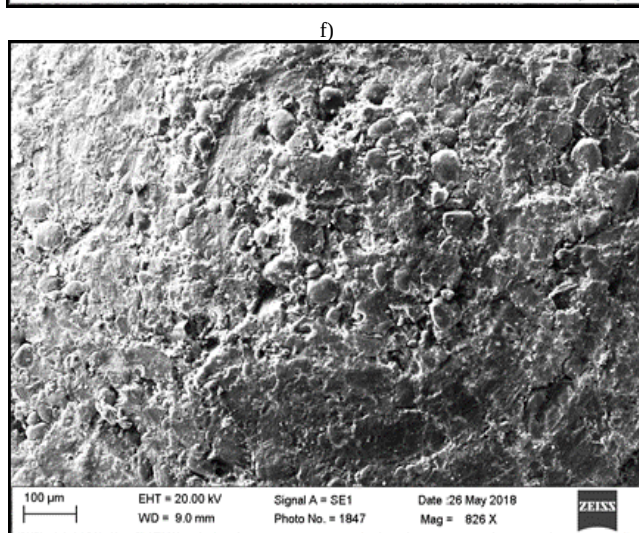
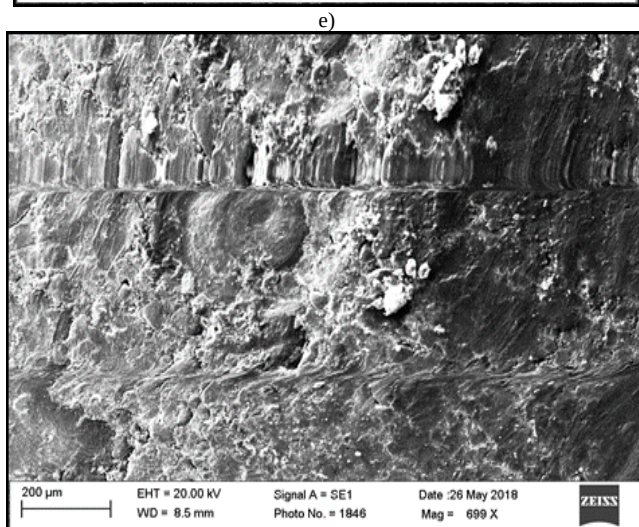
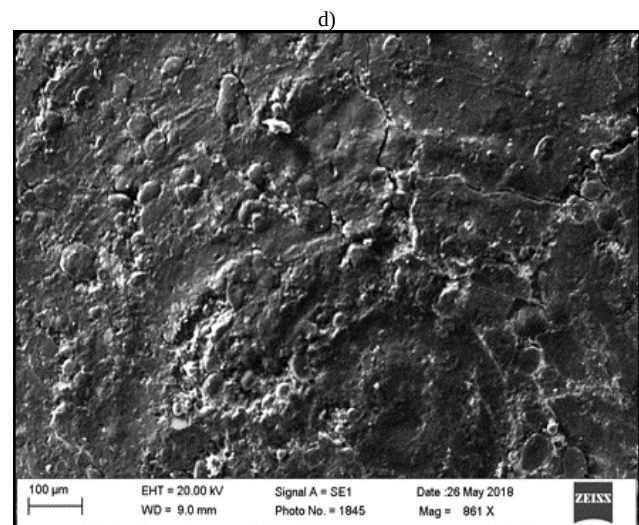
SEM is very helpful in studying the change in the surface topography and shape of the particles of pure drug and direct compression.

The formulation was further subjected for SEM analysis.

The SEM for all formulations is shown in Figure 5. SEM study indicated that pure drug particles were irregular in shape. The order of increasing roughness of tablet surface is F1<F2<F3<F4<F5<F6. The increasing roughness might be responsible for higher % of drug release as the surface area increases roughness of tablet surface. [21].

Figure. 5. Scanning electron micrograph of (a) Formulation F1; (b) Formulation F2 (c) Formulation F3 (d) Formulation F4 (e) Formulation F5 (f) Formulation F6.





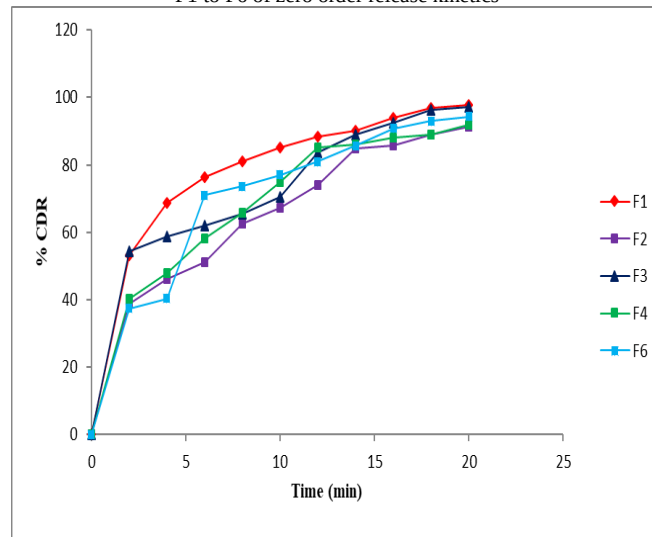
In- vitro dissolution study

In-Vitro dissolution study was carried out in PBS (pH 6.8) for one hr. The temperature was maintained at $37 \pm 0.5^\circ\text{C}$ and paddle rotating speed at 50rpm. Percent cumulative drug release was calculated for each formulation to obtain the drug release profile for the formulations.

The Percent cumulative drug release was found to be 97.735%, 91.342%, 97.307%, 91.774%, 56.246%, and 94.329% for

the formulations F1, F2, F3, F4, F5 and F6 respectively (Figure 6). Formulation F1 showed the highest drug release (97.735%), while the formulation F5 showed the least drug release (56.24%).

Figure 6: Comparative in- vitro drug release study graph of all formulations F1 to F6 of zero order release kinetics



DISCUSSION

In the current research six formulations of mouth dissolving tablets of oseltamivir phosphate were ready by direct compression method utilizing SSG as a super disintegrating agent. The manufactured tablets were then subjected to different assessment parameters such as Drug content analysis, Micromeritics evaluation, FTIR, Scanning Electron Microscopy and In-vitro dissolution study etc. All the results were found to be within acceptable ranges. Drug content analysis of all the formulations was done using PBS (pH 6.8) as medium at λ_{max} 221nm. The formulation F6 prepared using SSG 50mg and SLS 10mg showed the higher drug content (98%), while the formulation F2 showed the least drug content (92%). It was observed that with the increase in SSG concentration, the drug content was also increased. Drug content was found to be uniform among the all formulation and ranged from 92% to 98%. Micromeritics studies showed that the formulation F5 showed the highest bulk density and the tapped density values, which indicates more efficient packing and good compaction capability with less interparticle voids. Carr's index and Hausner's ratio values was found to be within the acceptable range. Angle of repose showed good flow properties. SEM study indicated that pure drug particles were irregular in shape. The order of increasing roughness of tablet surface is $F1 < F2 < F3 < F4 < F5 < F6$. The increasing roughness might be responsible for higher % of drug release as the surface area increases roughness of tablet surface.

All the formulated (F1 to F6) tablets breezed through weight variety assessment as the % weight variety was inside the IP furthest reaches of $\pm 7.5\%$ of the weight.

The normal thickness of the all formulation was observed to be 2.24

mm and inside the restriction of standard Pharmacopoeia. The hardness of the tablet was observed to be 2.8 to 3.3 kg/cm². The most extreme friability of the formulation was observed to be 0.4%. The base friability of the plan was observed to be 0.3%. The % friability was under 1% in every one of the plans guaranteeing that the tablets were mechanically stable.

The tablets showed disintegration time less than specific limit (3 min) for mouth dissolving tablets. In-vitro dissolution study was carried out in PBS (pH 6.8) for one hrs. The Percent cumulative drug release was found to be 97.735%, 91.342%, 97.307%, 91.774%, 56.246%, and 94.329% for the formulations F1, F2, F3, F4, F5 and F6 respectively. Formulation F1 showed the highest drug release (97.735%), while the formulation F5 showed the least drug release (56.24%). Finally, it was concluded that SSG, SLS, D-mannitol, starch, lactose, and talcum can be successfully used in the formulation of Oseltamivir phosphate mouth dissolving tablets.

In this manner, mouth dissolving tablets of oseltamivir phosphate were effectively ready by utilizing direct compression method. The formulation will clearly upgrade bioavailability, increment patient consistence, display fast beginning of activity, low dosing and reduces incidental effects, in addition it shows great stability and every one of the components referenced will leads toward its notoriety sooner rather than later.

CONCLUSION

From the above work it was reasoned that the plan of the Oseltamivir Phosphate was observed to be more achievable than the traditional one, the super disintegrates utilized in the formulation were builds the water dissolvability of the medication. As we realize that the Oseltamivir Phosphate have the issue of oral bioavailability, by utilizing super disintegrate the oral bioavailability may upgraded up to it require limit. Here in the current work the utilization of SSG at the conc. 4.18- - 20.92mg give the great formulation drug discharge with better mechanical strength, consequently we can say that a novel orally quick deteriorating tablet of oseltamivir phosphate may accomplish great plan capacity for drug maker by utilizing these ingredients.

CONFLICT OF INTERSET

There is no conflict of interest.

ABBREVIATIONS USED

- FDF: Fast Dissolving Films; FDOFs: Fast Dissolv-ing Oral Films; CPZ: Chlorpromazine;
- HPMCE: 5- Hydroxy Propyl Methyl Cellulose Ethocel-5;
- HPMCE-15: Hydroxy Propyl Methyl Cellulose Ethos -cel-15;
- PVA: Poly Vinyl Alcohol.

SUMMARY

- OFDT of Oseltamivir Phosphate was prepared by direct compression method using SSG as a super disintegrating agent

with lactose, talcum, mannitol, SLS and starch. The prepared tablets were then subjected to various evaluation parameters such as Drug content analysis, Micromeritics evaluation, FTIR, Scanning Electron Microscopy and In-vitro dissolution study etc.

- In the present work the use of SSG at the conc. 4.18--20.92mg give the good formulation drug release with better mechanical strength, thus we can say that a novel orally fast disintegrating tablet of oseltamivir phosphate may achieve good formulation capability for pharmaceutical manufacturer by using these ingredients.

REFERENCE

1. Habib W, Khankari R, Hontz J, 2000. Fast-dissolving drug delivery systems, critical reviews in therapeutics, Drug Carrier Systems, 17(1), 61-11.
2. Seager H, 1998. Drug delivery products and Zydis fast dissolving dosage form J Pharm Pharmacol, 50, 375-7.
3. Kuchekar BS, Atul, Badhan C, Mahajan HS, 2003. Mouth dissolving tablets, A novel drug delivery system, Pharma Times 35, 7-9.
4. Deshmukh VN, 2012. Mouth Dissolving Drug Delivery System, A Review, Int J Pharm Tech, Res, 4(1), 412-9.
5. Indian pharmacopeia vol-1st, 7th edition, 2014. Indian pharmacopeia publishing, 503.
6. Ashish P, Harsoliya MS, Pathan JK, Shruti S, 2011. A Review-Formulation of Mouth Dissolving tablet, Int J Pharm Clin, Sci 1(1), 1-8.
7. Indian Pharmacopoeia, Vol-2, 1996. The Controller of Publication Delhi, p-735.
8. Khan S, Kataria P, Nakhat P, Yeole P, 2007. Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets, AAPS Pharm Sci Tech, 8(2), 46.
9. Lachman L, Liberman H, Kanig J, 1987. The theory and practice of industrial pharmacy, 3rd edn, Varghese Publishing House, Mumbai, 297.
10. United States Pharmacopoeia USP25 NF20, 2002. The Official Compendia of Standards, First annual Asian edn, Rockville MD, United States Pharmacopoeial Convention Inc, 36.
11. Wilson CG, Washington N, Peach J, Murray GR, Kennerly J, 1987. The behavior of a Fast dissolving dosage form (Expidet) followed by gamma scintigraphy, Int J Pharm, 40 (1-2), 119-4.
12. Prajapati BG, Patel RP, Patel SN, 2011. Formulation, evaluation & optimization of orally disintegrating tablet of cinnarizine using sublimation method, Bio phys, 38, 4089-92.
13. Chandana CH, Kumar YG, Vishnu YV, Madhuri MM, 2014. Metoprolol Succinate Sustained Release Matrix Tablets-Formulation Development and Invitro Evaluation, International Journal of Pharmacy and Pharmaceutical Sciences, 481-6.
14. Indian Pharmacopoeia, Vol-2, 1996. The Controller of Publication Delhi, p-735.
15. Jain CP, Naruka PS, 2009. Formulation and evaluation of fast dissolving tablets of valsartan, Int J Pharma, Pharma Sci, 1 (1), 219-7.
16. Matt Carter, Jennifer Shieh, 2015. In Guide to Research Techniques in Neuroscience, (Second Edition).

17. Stokes, Debbie J, 2008. Principles and Practice of Variable Pressure Environmental Scanning Electron Microscopy (VP-ESEM), Chichester John Wiley & Sons, ISBN, 978-0470758748.
18. Sangale Shamrao S, Vaibhav K, Mahale NB, & Chaudhari SR, 2015. Formulation development and evaluation of or dispersible tablet of diclofenac sodium by sublimation technique. World Journal of Pharmaceutical Research, 5 (2), 1300-6.
19. Lachman L, Liberman H, Kanig J, 1987. The theory and practice of industrial pharmacy, 3rd edn, Varghese Publishing House, Mumbai, 297.
20. Allen LV, Wang B, 1997. Particulate support matrix for making a rapidly dissolving tablet, US Patent, 5595761.

How to cite this article

Peeush Singhal, Piyush chamola, Vijay Jyoti Kumar, Sarvesh Kumar, Abhiram Rout, 2021. Oseltamivir Phosphate, Mouth Dissolving Tablet, Scanning Electron Microscopy, Super Disintegrating Agent. Jour. of Med. P'ceutical & Allied. Sci. V 10 - I 6, 1479, P- 3781 - 3788. doi: 10.22270/jmpas.V10I6.1479