https://doi.org/10.48047/AFJBS.6.Si4.2024.4855-4870

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

FORMULATION AND IN-VITRO EVALUATION OF SUBLINGUAL TABLET

Ankit Yadav*, Dr. Nitin Nama, (Prof.) Dr. M.K. Gupta, Alok Kumar
Career Point School of Pharmacy, Career Point University, Kota, Rajasthan, India
Email – anikt9616002286@gmail.com

Article History
Volume 6, Issue Si4, 2024
Received: 1 July 2024
Accepted: 20 July 2024
Doi:
10.48047/AFJBS.6.Si4.2024.4855-4870

ABSTRACT

Any medication delivery system's objective is to swiftly attain and then maintain the intended drug concentration by administering a therapeutic amount of the medication to the appropriate area in the body. For the course of therapy, The drug delivery system should be used to supply the medication at a rate determined by the body's requirements. Even the best new therapeutic substance in the world won't be particularly helpful without an appropriate delivery system. Tablet delivery methods enable the creation of complex extended or modified release dose forms as well as straightforward immediate release formulations. Delivering the medicine to the site of action in the right amount and at the right rate is the primary goal of the drug delivery system. It must, however, also fulfil additional crucial requirements, such as the capacity to be mass-produced in a manner that guarantees consistency of content and stability in terms of both chemistry and physical properties. Because solid dosage forms have been around for a very long period, they are very common.

Keywords: Sublingual Tablet, Homogeneity, Therapeutic, Drug Delivery.

Introduction

Oral administration.

Since its formulation flexibility, patient compliance, and ease of administration, among other advantages, the oral route of drug delivery is strongly recommended.[1] Historically, the most popular way to provide medication has been orally. There is a slight chance of harm at the site of administration, but there is no sterility in concern [2].It is difficult to establish a steady state condition because of the normal plasma concentration-time profile that has peaks and troughs.[3]

Because oral administration can result in patient compliance, it is the preferred form of administration. formulation flexibility, and dosage form flexibility. The drug's formulation and the various pH levels it will encounter during its passage through the digestive system, as well as the gastrointestinal tract's motility and the enzyme system, must all be taken into account. The progressive release of drug into the gastrointestinal tract is accomplished by most oral long-term delivery systems through a combination of dissolution, diffusion, or both. The best possible result of a continuous delivery method is zero-order medication release. yields a blood level time profile that resembles the results of continuous constant rate infusion. A comparison is made between the medication concentration patterns in plasma fora prolonged-release formulation, a zero-order long-term release formula, as well as a standard tablet or capsule shape.[4,5]

Benefits of sustained-release formulations

a) Decrease in the frequency of consumption. b) Minimiseadverse reactions consistent and gradual release of medication over aperiod of time. c) Improved adherence from patients.[6]

Omeprazole.

The first medication in a recently developed family class drugs referred to as acid pump inhibitors is omeprazole. These medications lessen both induced and basal acid secretion, irrespectivevia regulating the last stage of the stimulus's generation of stomach acid of the acid secretory pathway. Instead of using Patients using 800 or 1000 mg of cimetidine daily, When using omeprazole once daily at a dose of 20 mg, duodenal or stomach ulcers heal more rapidly and completely than when taking ranitidine 300 mg at bedtime or 150 mg twice a day. Omeprazole is a useful medication if histamine H2-receptor therapy is not working for a patient.

antagonist medicine; after taking omeprazole 40 mg/day for 4–8 weeks, the majority of ulcers healed.Maintenance treatment with 20 or 40 mg of omeprazole per day has been used for peptic ulcers with very few recurrences.ulcer disease during the preceding five years. 20 or 40 mg/day of omeprazole provides greater recovery and symptom alleviation than ranitidine in 80% of individuals with erosive or ulcerative oesophagitis after 4 weeks. More than 80% of individuals with severe oesophagitis or reflux who do not answer well to H2- receptor antagonists recovered in less than 8 weeks. Over the course of a year, over 80% of patients who get maintenance medication at a daily dosage of 20 mg are able to avoid recurrence.

The best medication for lowering stomach acid production in those with Zollinger-Ellison syndrome is thought to be omeprazole. During therapy, basal acid production can be effectively reduced reach goal values (> 10 mmol/h; for patients, less than 5 mmol/h)undergoing partial gastrectomy or severe oesophagitis). with daily doses of 20 to 360 (median 60 to 70 mg). [7,8,9]

Materials and methodology

MaterialsRequired

Table1:Required Chemicals List

S.No.	Chemicalname
1	KyroneT314
2	Sodiumstarchglycolate

3	Crospovidone
4	Magnesiumstearate
5	Mannitol
6	Fructose
7	Talc

Table2:List of instrumentsrequired

S.No.	Instrumentname
1	Colorimeter
2	UV-VisSpectrophotometer
3	WeighingBalance
4	Hotairoven
5	Glasswares
6	TabletPunchingMachine
7	FT-IR
8	Capillarytube
9	Waterbath
10	Monsantohardnesstester
11	VernierCalliper

Methodology:

Pre-formulationstudies:

Pharmaceuticalcharacterizationinvolvesstudyingtheofatherapeutic component both on its own and when mixed with other substances calledexcipientsPrior to formulation, testing is primarily done to collect relevant data that will help the formulator create products that are suitable for large-scale production.

Organolepticproperties:

Fortheassessmentofproductqualityinthefoodandpharmaceuticalsectors,organolepticattributesliketaste,texture,appearanceandsmell arecrucial.

Meltingpoint:

A capillary tube that was open on both ends and filled with 0.1 grammes of themedicationwasplaced inthe melting pointdevicealongsideathermometer.

UV-VisSpectralAnalysis:

Lambdamaxdetermination:

Before being used, the 0.01-gram sample disappeared in10 millilitres of purified water andlet To stand at room temperature for an entire day.Following the filtering of the samples, absorbance measurements were taken at different 200–400 nm wavelengths.[10,11,12]

Standardcalibrationcurvepreparation:

100mg/mlstocksolutionwasprepared,theworkingsolutionofdifferentconcentrationswas prepared,and the absorbancewastaken atlamdamax.

Differentsolvents:

After dissolving the 0.01-gram medication in 10 milliliters of various solvents, The incubation period was set at Room temperature for twenty-four hours. **Next** filtering the solution, absorbance measurements were made at 210 and 230 nm.

DifferentpH:

After the 0.1g medication was dissolved in 100ml of methanol at various pH values, it was given time to develop a full day at the standard temperature. After filtering the solution, absorbance measurements were made at 230 and 210 nm.

FTIR:

An FT-IR spectrometer-8400S (Shimadzu, Japan) will be used to produce FT-IRspectra for the materials. With 20 co-added scans and a resolution of 4.0 cm1, The FT-IR spectra's range is 400–4000 cm–1. will be obtained. By carefully mixing samples with KBr at a 1:100 ratio, thesampleswill beproduced in KBr discs.

Formulation:

Omeprazole sodium Using the direct compression method, sublingual tablets were created. process, which also included the use of other super disintegrants, including Kyrone T-314 and Cross povidone. Theexactdosageofthemedication and all the constituents were measured and blended in a certain order aftercareful blending of the drug and other elements.The resultant mixture was subsequentlyfiltered, individually. After undergoing a screening process, the hardness of the materialswas adjusted and they were compressed into tablets, with each tablet weighing 120mg.A Cadmach multi tablet compression machine, a rotating tablet machine with 12 stations, was used to complete the operation.

Table3:Excipients chosen for the prototype's formulation

.

FUNCTION	EXICIPIENT
Superdisintegrant	KyroneT314
Superdisintegrant	Sodiumstarchglycolate
Superdisintegrant	Crospovidone
Lubricant	Magnesiumstearate
Diluent	Mannitol
Sweeteningagent	Fructose
Glidant	Talc

Table4:Formulation Development: Omeprazole Sodium Sublingual Tablets

FORMULA CODE	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Rabeprazole	20	20	20	20	20	20	20	20	20	20	20
Crosspovidone	40	20	37	25	36	24	23	19	20	-	-
Sodium starch glycolate	-	-	27	38	-	-	20	22	20	37	25
Kyrone T-314	-	19	-	-	28	38	21	23	22	27	39
Mannitol	43	44	20	20	20	21	20	20	22	20	20
Fructose	10	10	10	10	10	10	10	10	10	10	10
MagnesiumStearate	4	3	3	4	3	4	3	3	3	3	3
TALC	3	4	3	3	3	3	3	3	3	3	3
TOTAL WEIGHT	120	120	120	120	120	120	120	120	120	120	120

***The units of measurement for all quantities are milligrammes (mg).**

InvitroEvaluationStudies

The following metrics will be assessed for the prepared omeprazole tablets:

i. **Weightvariation:**Weighing each tablet individually and then all at once allowed us to calculate the average weight of the ten.

ii. **Hardness:** A Pfizer hardness tester was used to determine how hard the pills were. For

mechanical stability, 3-5 kg of tablet hardness is considered to be sufficient.

iii. **Thickness:** A micrometre screw gauge used to measure the buccal pills' thickness. Ten distinct tablets from each batch were used to calculate the average thickness.

iv. **Friability:**A Roche Friabilator was used to evaluate the tablets for friability. In order to conduct this test, six tablets were weighed, spun at 25 revolutions per minute in the Friabilator's plastic chamber to experience both shock and abrasion, and then the tablets were dust-treated and weighed again.

v. **Drug content:**The pH 6.8 phosphate buffer was utilised.to extract the from five tablets (n = 5), each of which was weighed individually. The combination was then filtered with Paper filter from Whatman. The absorbance was calculated at lambda max Employing An ultraviolet/visible double beam spectrophotometer, the Shimadzu UV-1601 with an appropriate dilution.

vi. **Wetting time:**The paper was completely moistened with distilled water, and any leftover water was drained from the dish. The amount of time it took for the water to diffuse throughout the entire tablet from the wet absorbent paper was then measured using a timer.

Results and Discussions

Pre-FormulationStudies

Table5:Organolepticpropertiesofdrug

S.No.	Tests	Outcome
1	Physicaldescription	Solidpowder
2	Color	White
3	MeltingPoint	155°C

Table6:Omeprazole sodium lamda max in phosphate buffer, pH 6.8

S.No.	Wavelength(nm)	Absorbance
1	200	0.418
2	220	0.058
3	240	0.069
4	260	0.055
5	280	0.085
6	300	0.458
7	320	0.04
8	340	0.09
9	360	0.007
10	380	0.005
11	400	0.002

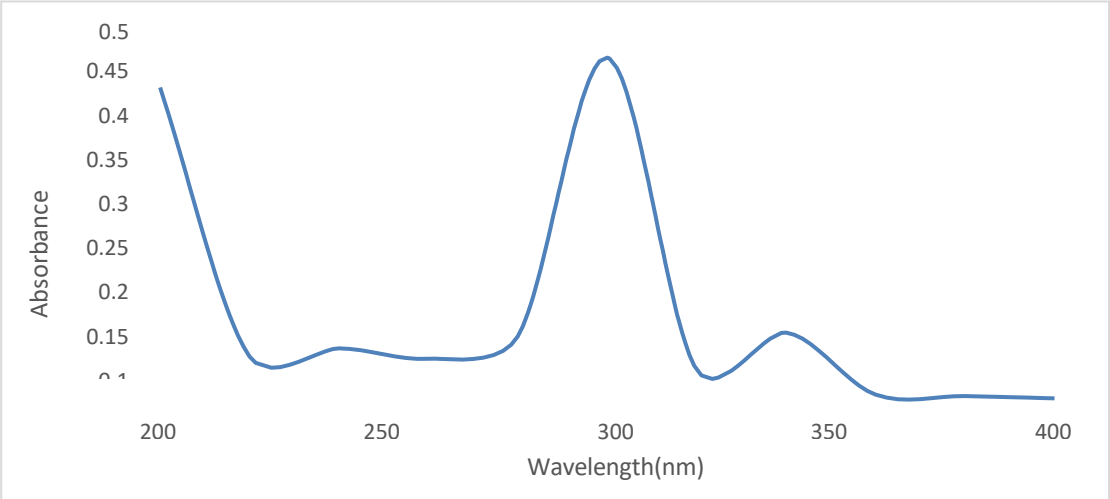


Fig.2:omeprazole sodium lamda max in phosphate buffer (6.8).

Calibrationcurve: Omeprazole was dissolved in methanol solvent to make a 10 mg/ml solution, after which it was incubated for one hour at 45°C and one more hour at 37°C. The sample was filtered usingmicrofilterandthestandardcurvewaspreparedbytakingabsorbanceat300nmofdifferentconcentrationsof omeprazole.

Table7:Calibrationcurve

S.No.	Concentrations(ug)	Absorbance
i	10	0.01
ii	20	0.045
iii	40	0.089
iv	60	0.112
v	80	0.145
vi	100	0.199

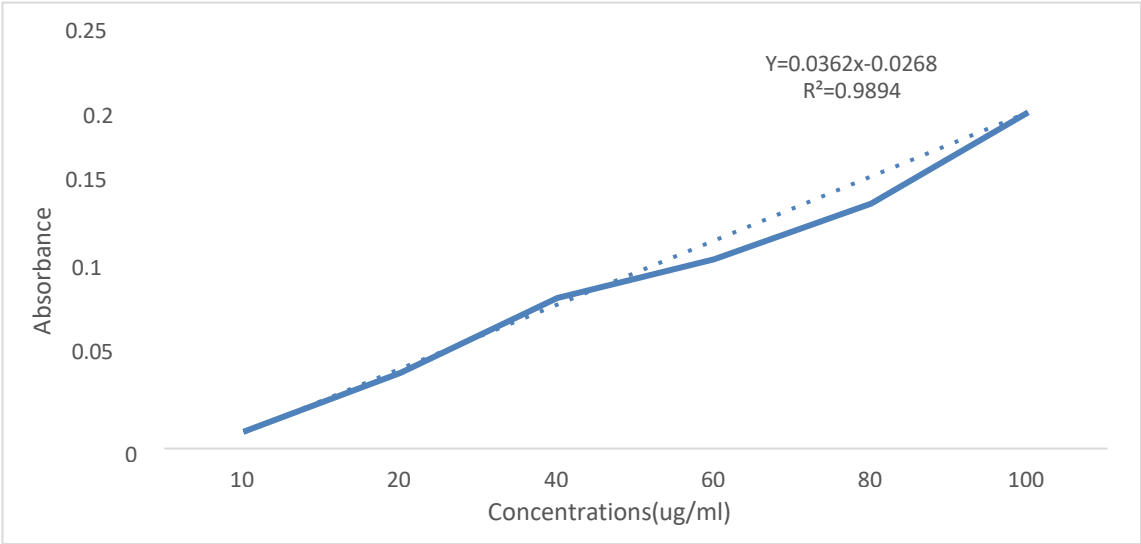


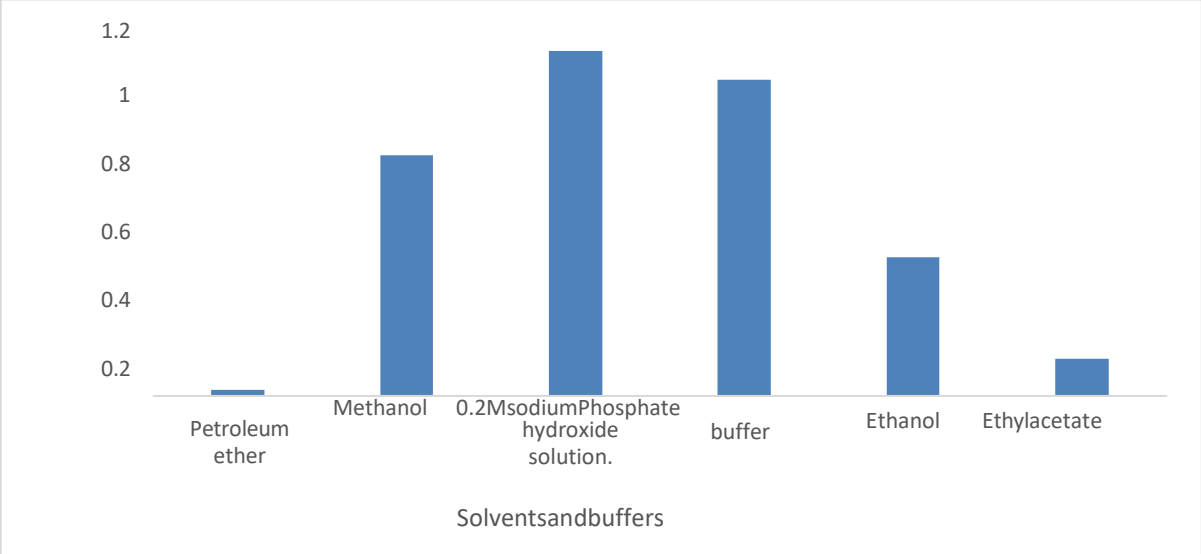
Fig.3 :Calibrationcurve

Solubilityindifferentsolvent:

The 100 mg/ml drug was allowed to dissolve in respective solvents andbuffer. Then incubated at 45℃ for 1 hour and again incubated at 37℃. Thesample was filtered using microfilter and the standard curve was prepared bytakingabsorbanceat 300nm ofdifferentconcentrations ofomeprazole.

Table8:Drugsolubilityatdifferentsolvents

S.no.	Solvents	Absorbance
1	Petroleumether	0.02
2	Methanol	0.78
3	0.2Msodiumhydroxidesolution.	1.12
4	Phosphatebuffer	1.025
5	Ethanol	0.45
6	Ethylacetate	0.12



Figiure4:Solubilityatdifferent solvent

FTIRSpectroscopy

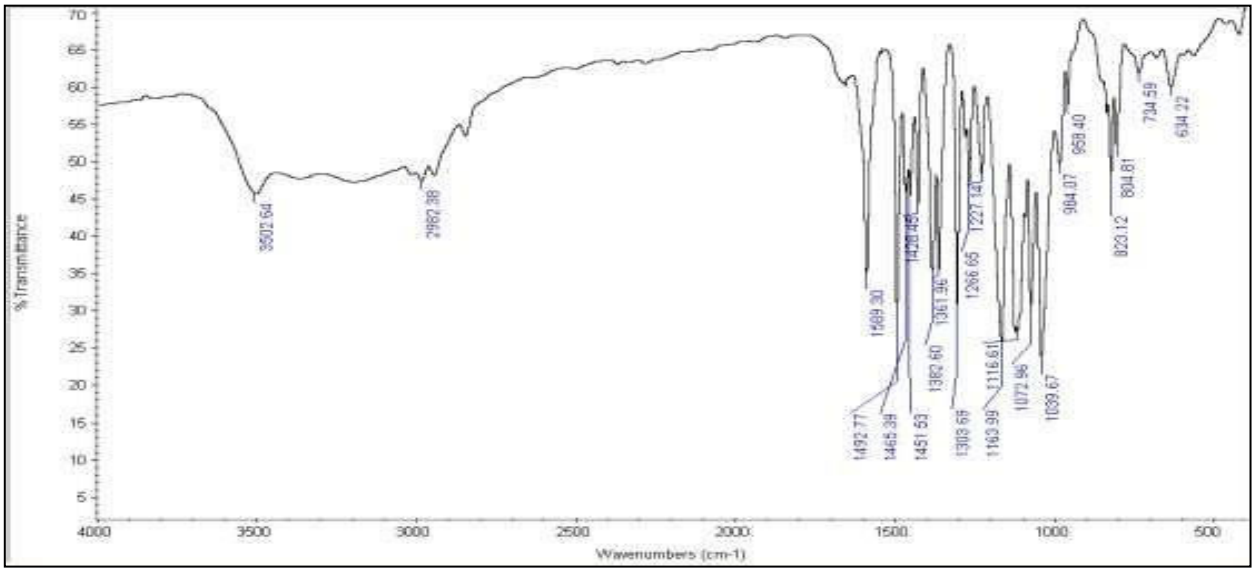


Fig.5:FT-IR spectra were used to determine the FT-IR of the omeprazole sodium.

Table9 :The physical makeup of Formulation F7, the medicine in combination with the excipients, and the FT-IR characteristic peak of omeprazole sodium.

Si	FUNCTIONAL GROUP	IR RANGE (cm^{-1})	IROBSERVEDPEAKS		
			Pure drug	Drug+Cross povidone	Drug ssg
1	N-H	3400-3500	3502.64	3496.92	3561.10
2	C-H	2960-2850	2982.38	2946.13	2970.13
3	C=N	1630-1690	1589.30	1588.31	1589.23
4	C=C	1450-1600	1492.77	1492.63	1492.76
5	C-O	1310-1410	1303.69	1303.60	1303.67
6	S=O	1050-1400	1116.61	1118.67	1124.02
7	C-F	1000-1400	1072.96	1071.93	1073.00

Table10:Omeprazole sodium drug's distinctive peak in FT-IR, drug + excipients, and formulation F7's physical mixture

SI	FUNCTIONAL GROUP	IRRANGE (cm^{-1})	IR OBSERVED PEAKS		
			Drug +KyroneT-314	Drug+Mannitol	Physical mixture formulation
1	N-H	3400-3500	3497.24	3399.93	3400.87
2	C-H	2960-2850	2970.94	2970.87	2916.78
3	C=N	1630-1690	1589.18	1589.33	1588.48
4	C=C	1450-1600	1492.70	1492.80	1492.61
5	C-O	1310-1410	1303.73	1303.31	1303.29
6	S=O	1050-1400	1124.19	1115.76	1107.64
7	C-F	1000-1400	1072.29	1076.82	1078.44

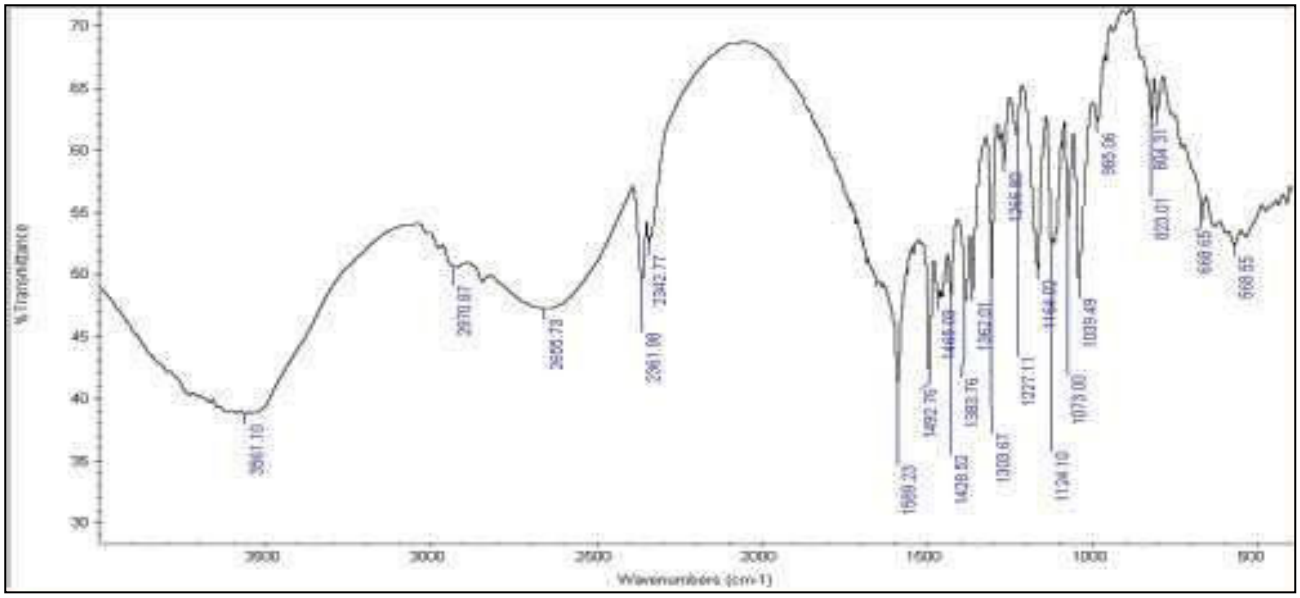
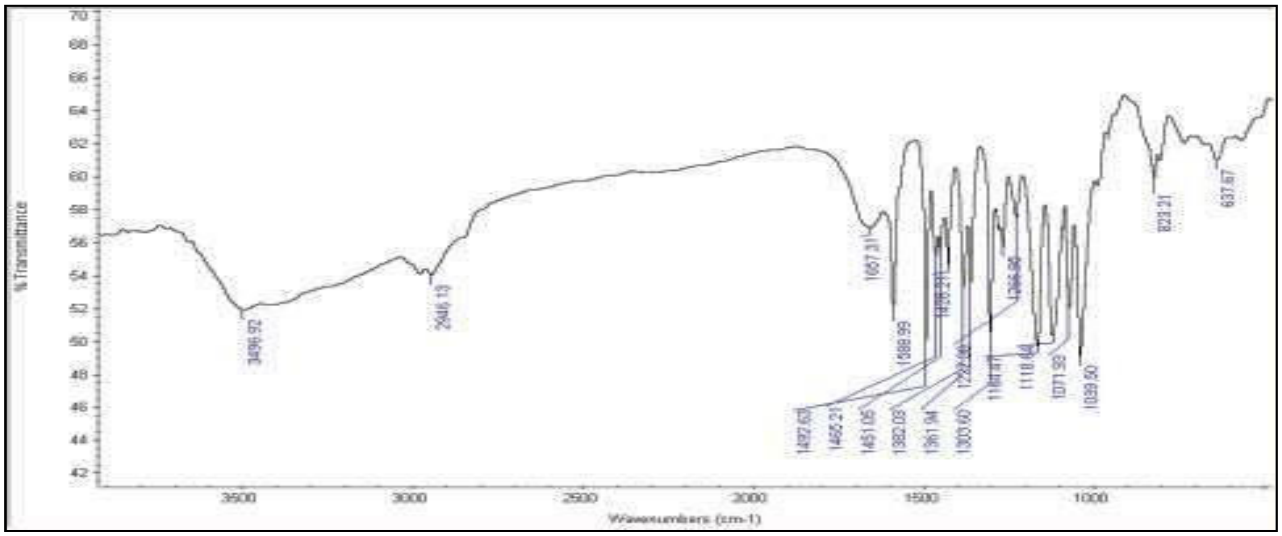


Fig.5:Drug's infrared spectrum with cross povidone



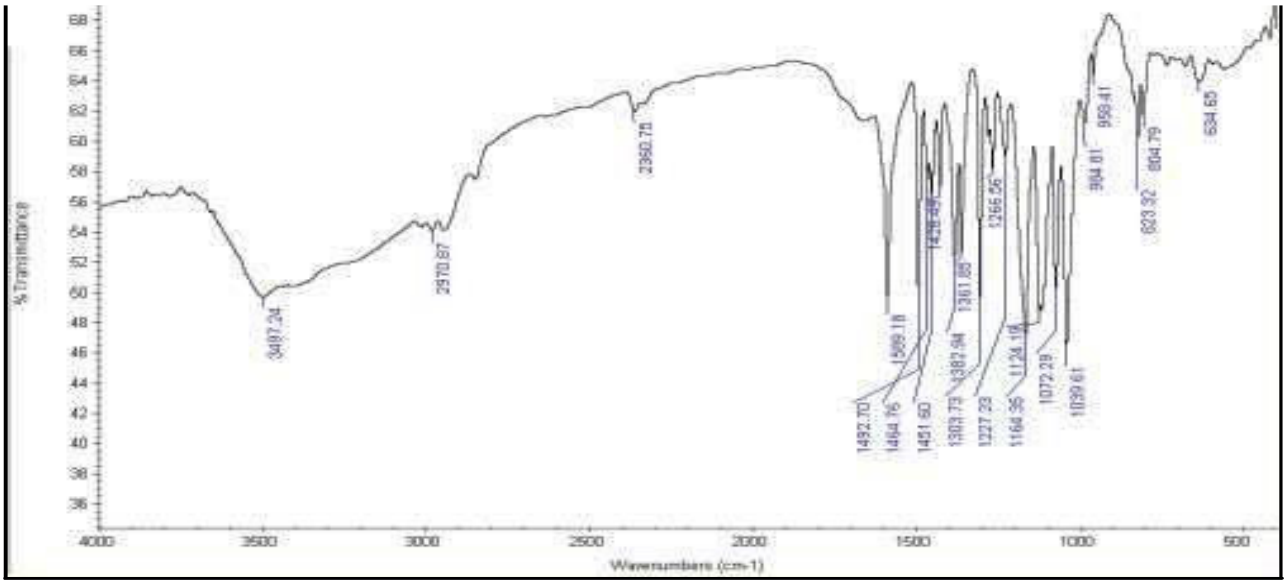


Fig.7:The medication Kyrone T-314's infrared spectrum

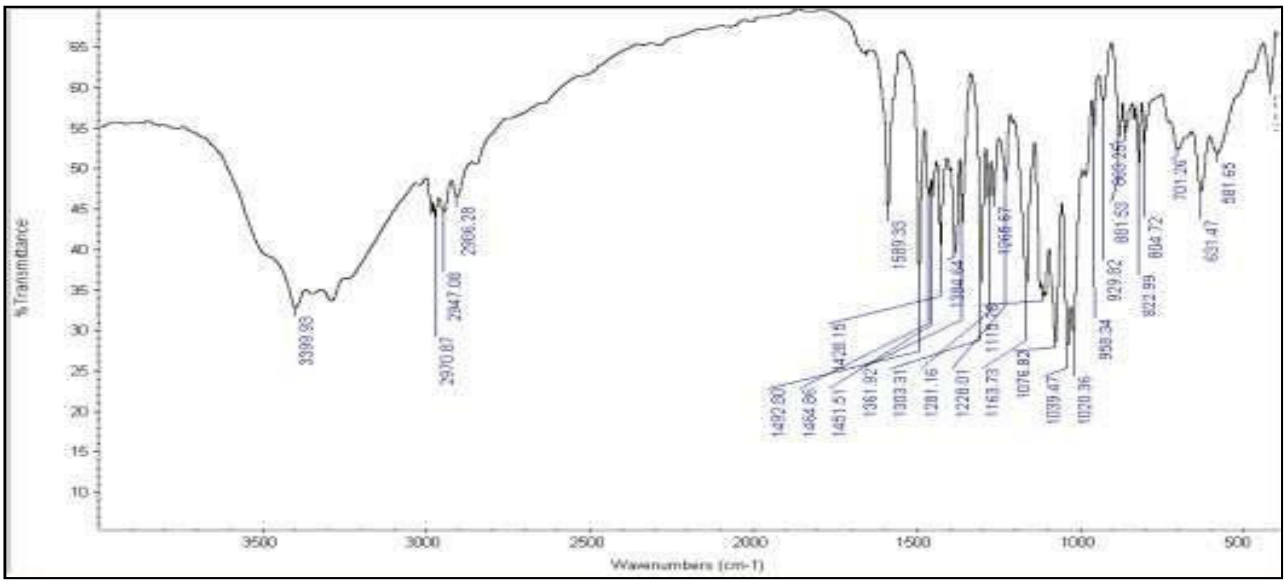


Fig.8:IR spectra of mannitol-containing drug.

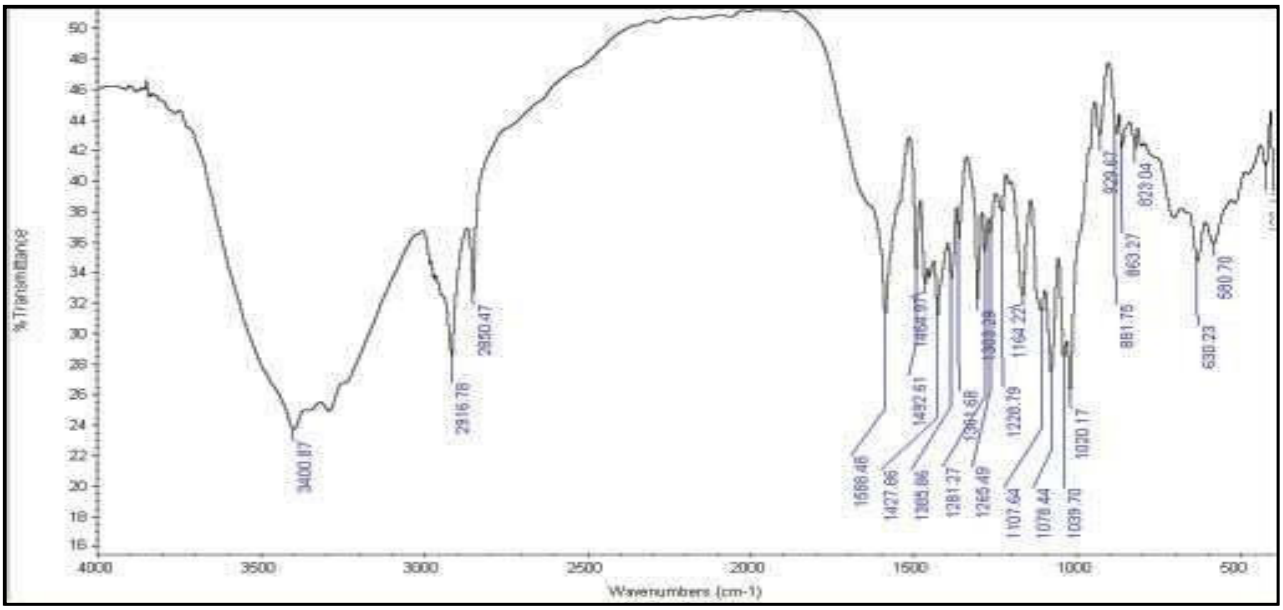


Fig. 9:Spectral analysis of Formulation F7

FormulatedTablets

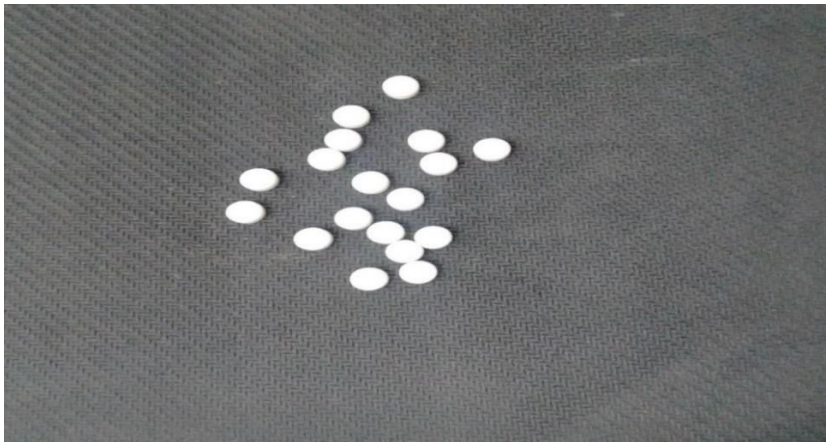


Fig.10:Formulatedtablets

Analysis of combined properties of omeprazole sodium sublingual formulation

Table11:Pre-Compression Parameter Outcomes.

Code	Bulk density g/cm^3	Tapped dencityg/cm^3	Carr'sindex%	Hausner'sratio	Angle ofrepose(°)
F1	0.522±0.0951	0.63±0.1201	16.66±0.033	1.20	28.57±0.041
F2	0.528±0.1012	0.625±0.0344	15.491±0.09	1.19	28.20±0.0675
F3	0.529±0.0745	0.621±0.0699	14.831±0.05	1.18	27.87±0.0513
F4	0.524±0.0896	0.633±0.0911	17.242±0.04	1.20	26.23±0.0792
F5	0.522±0.0935	0.625±0.1133	16.379±0.03	1.20	27.94±0.0842
F6	0.477±0.1122	0.556±0.1088	14.231±0.04	1.17	27.62±0.0992
F7	0.51±0.1074	0.587±0.077	14.90±0.107	1.17	25.52±0.0212
F8	0.524±0.0999	0.621±0.0744	15.640±0.09	1.19	25.87±0.0443
F9	0.53±0.0944	0.61±0.0433	13.330±0.12	1.16	23.14±0.0421
F10	0.523±0.0866	0.622±0.0211	15.960±0.04	1.19	27.63±0.0425
F11	0.478±0.0866	0.568±0.099	15.52±0.025	1.19	25.889±0.0423

Pre-formulation studies

Excipient and active pharmaceutical ingredient blends were created for every kind of formulation and evaluated based on several criteria, as previously stated. The tapped density was found to be between 0.555 and 0.632 g/cm3, while the bulk density was between 0.476 and 0.529 g/cm3. The two previously stated density data were used to calculate Carr's compressibility index. All powder mixes had good flow qualities, according to data on flow ability and compressibility, which ranged from 14.9% to 17.24%. The angle of repose further demonstrated each powder blend's superior flow characteristics. The angle of repose ranged from 23.12°–28.56°. Less than a 30-degree angle of repose denotes good flow characteristics.

Omeprazole sodium sublingual tablet formulation

The procedure described in methodology section 4 was used to fix eleven formulations of sublingual tablets containing omeprazole sodium. A range of journals and research publications were used to select the formulation techniques.As superdisintegrants, cross povidone and sodium starch glycolate are employed, mannitol is used as a diluent, and fructose is used as a sweetener.

Tableting

By maintaining a consistent tablet press setting for all formulations, the homogeneous blends of tablet composition were compacted directly. In order to completely exclude any potential impact of these factors on the study, proper lubrication of powder mixes was necessary for the bottom punch to move freely

during the compression cycle and for the crushed tablets to be easily ejected.

Parameters for Post-Compression Evaluation

Table12:Organoleptic characteristics each formulation's flavor, color, and aroma.

RMULATIONCODE	ODOUR	TASTE	COLOURS
F1	Odourless	Sweet	White
F2	Odour less	Sweet	White
F3	Odour less	Sweet	White
F4	Odour less	Sweet	White
F5	Odour less	Sweet	White
F6	Odour less	Sweet	White
F7	Odour less	Sweet	White
F8	Odour less	Sweet	White
F9	Odour less	Sweet	White
F10	Odour less	Sweet	White
F11	Odour less	Sweet	White

Table13:Post-compressionparameterresults.

Code	Drugcontent(%)	sintegration Time(sec)	WettingTime(Sec)	%CDR
F1	93.51±0.57	57	42	62.678
F2	95.00±0.42	41	39	81.986
F3	96.85±0.32	37	36	86.122
F4	95.79±0.27	39	36	83.454
F5	97.01±0.89	35	32	87.917
F6	96.15±0.42	39	34	85.937
F7	97.97±0.84	31	30	92.176
F8	97.35±0.42	33	32	90.117
F9	98.99±0.42	29	28	94.001
F10	96.31±0.16	49	39	75.203
F11	95.14±0.57	43	39	79.681

CODE	Weight variation (mg)	Hardness(kg/cm^2)	Thikness(mm)	Friability(%)
F1	119.91±0.22	3.02±0.10	3.12±0.01	0.39±0.15
F2	120.33±0.36	3.19±0.09	3.15±0.03	0.56±0.11
F3	120.21±0.49	3.16±0.04	3.18±0.03	0.77±0.09
F4	120.92±0.41	3.34±0.007	3.12±0.02	0.43±0.62
F5	120.16±0.32	3.15±0.05	3.32±0.01	0.42±0.44
F6	119.95±0.91	3.30±0.03	3.19±0.04	0.62±0.53
F7	120.09±0.99	3.06±0.10	3.19±0.01	0.34±0.20
F8	120.11±0.60	3.14±0.14	3.15±0.02	0.40±0.32
F9	120.01±0.59	3.05±0.05	3.15±0.01	0.27±0.06
F10	119.95±1.02	3.27±0.06	3.17±0.01	0.33±0.09
F11	120.03±0.59	3.16±0.04	3.14±0.01	0.66±0.09

Table14:Post-compressionparameterresults.

Thicknessoftablets

"Vernier callipers" were used to measure the thickness of each sublingual tablet formulation. It was found that All of the formulations' average thickness was betweenfive percent of the standard value, or the allowable deviation limit. Every formulation had a crown diameter of 6 mm**.**

Hardness

When assessing a tablet's resistance to breaking, abrasion, or cappingduring handling, keeping things in storage, andtransit prior to use, tablet hardness is an essential metric to consider. Since all formulations must dissolve on the tongue between 30 and 60 minutes, it was determined that all of the formulations' average hardnesses, ranging from 3.02 to 3.34 kg/cm2, were acceptable. For these formulations, excessive hardness is therefore not recommended. Out of all the formulations, F4 had the maximum hardness value (3.34±0.007 Kg/cm2), whereas F1 had the lowest hardness value (3.02±0.10 Kg/cm2) for the aforementioned parameters. All of the formulations had almost equal hardness and adequate hardness to provide good mechanical strength.

Friability

In order to assess the tablets' resistance to abrasion during handling, packing, and transportation, their friability is measured. All of the formulations' average percentage friability fell between 0.27% and 0.77%, falling within the standard's maximum 1% range. Accordingly, for the aforementioned parameters, the maximum friability was found for F3 to be 0.77% and the minimum friability for F9 to be 0.27%.

WettingTime

In order to provide insight into the tablet disintegration properties, wetting time is another crucial quantity that is related to water absorption. The timing of the wetting period matches the allowed the tablet to dissolve on the tissue paper in a petridish while it was stationary. Because the tablet is kept immobile beneath the tongue, this technique will replicate the disintegration that occurs in vivo. For every formulation, the average wetting time varied between 28 and 42 seconds. F1 and F9 displayed the largest wetting duration of 28 seconds and the lowest wetting time of 42 seconds, respectively.

WeightVariation

Because the contentflowed freely, uniform diefill with allowable variation in weight was obtained in tablets that met IP criteria. F4 had a maximum weight of 120.92±0.49 mg, and F1 had a minimum weight of 119.91±0.22 mg. For 120 mg tablets by I.P., the maximum permitted percentage weight variation is 7.5%; no formulation is going over this limit. Consequently, it was discovered that every composition complied with the IP rules.

DrugContent

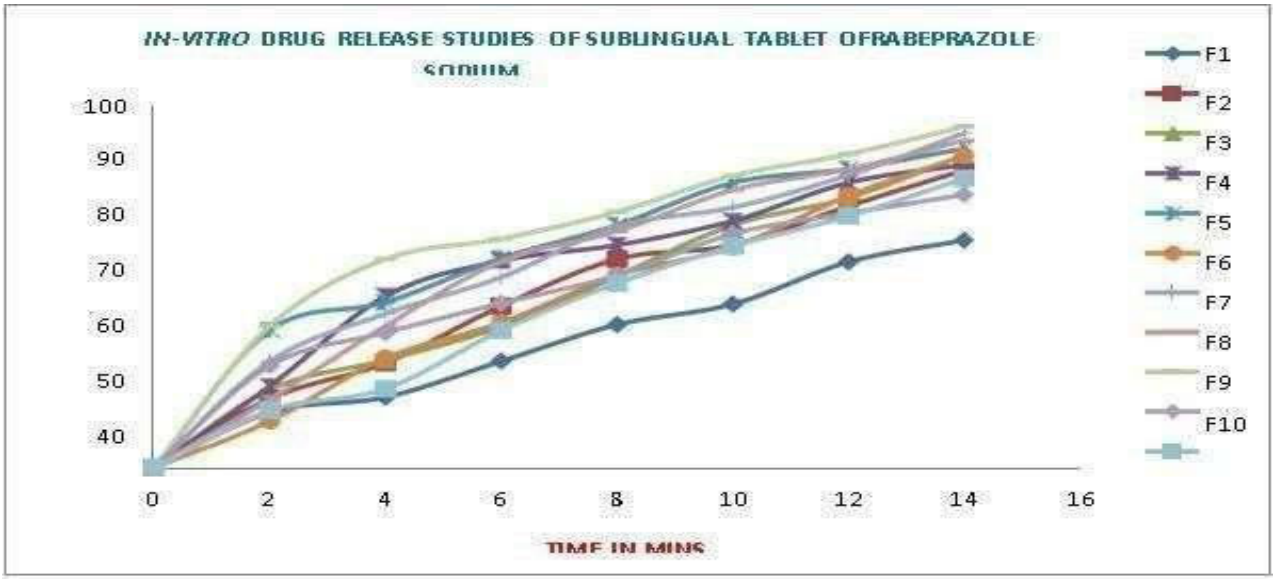
The methodology section 4 approach was followed to evaluate the drug content homogeneity of each sublingual tablet formulationTable No. 26 presents the findings. Each formulation's proportion of medication content was discovered to rangefrom 93.51±0.57%w/w to 98.99±0.42%w/w, all within recognised legal limits. F9's drug content ranged from 93.51±0.57%w/w in F1 to a high of 98.99±0.42%w/w.

In-vitrodisintegrationtime

The first phase of drug absorption from a solid dosage form following oral administration is called breakdown, and this was the primary focus of this study. Hardness affects the porosity of the matrix, which in turn affects the water's ability to travel through the matrix, making it a crucial factor that affects the disintegration process and has an effect on the disintegration time. All of the formulations had an average in vitro disintegration time of between 29 and 57 seconds.

Table15:*Omeprazole sodium sublingual tablet in vitro drug release investigations.*

TIMEIN MIN	%CUMULATIVEDRUGRELEASE					
	FORMULATIONCODE					
	F1	F2	F3	F4	F5	F6
2	15.28	18.98	21.53	22.38	37.84	12.84
4	19.40	28.85	29.62	47.27	45.52	30.17
6	29.32	44.50	38.88	57.00	57.66	39.94
8	39.39	57.45	52.78	61.30	66.80	52.93
10	45.04	61.29	66.82	67.97	78.48	60.77
12	56.67	72.07	74.36	78.51	82.28	74.93
14	62.67	81.98	86.12	83.12	87.91	85.93



TIME IN MIN	%CUMULATIVEDRUG RELEASE FORMULATIONCODE				
	F7	F8	F9	F10	F11
2	29.26	18.83	39.00	28.10	15.78
4	42.38	39.01	57.45	37.18	21.73
6	52.45	56.82	63.03	45.28	37.81
8	66.45	65.12	70.46	53.01	50.77
10	71.66	76.51	80.37	64.43	61.00
12	80.57	82.22	86.38	70.06	69.29
14	92.17	90.11	94.00	75.20	79.69

Fig.11: ***Drug release experiments on omeprazole sodium sublingual tablet in vitro.***

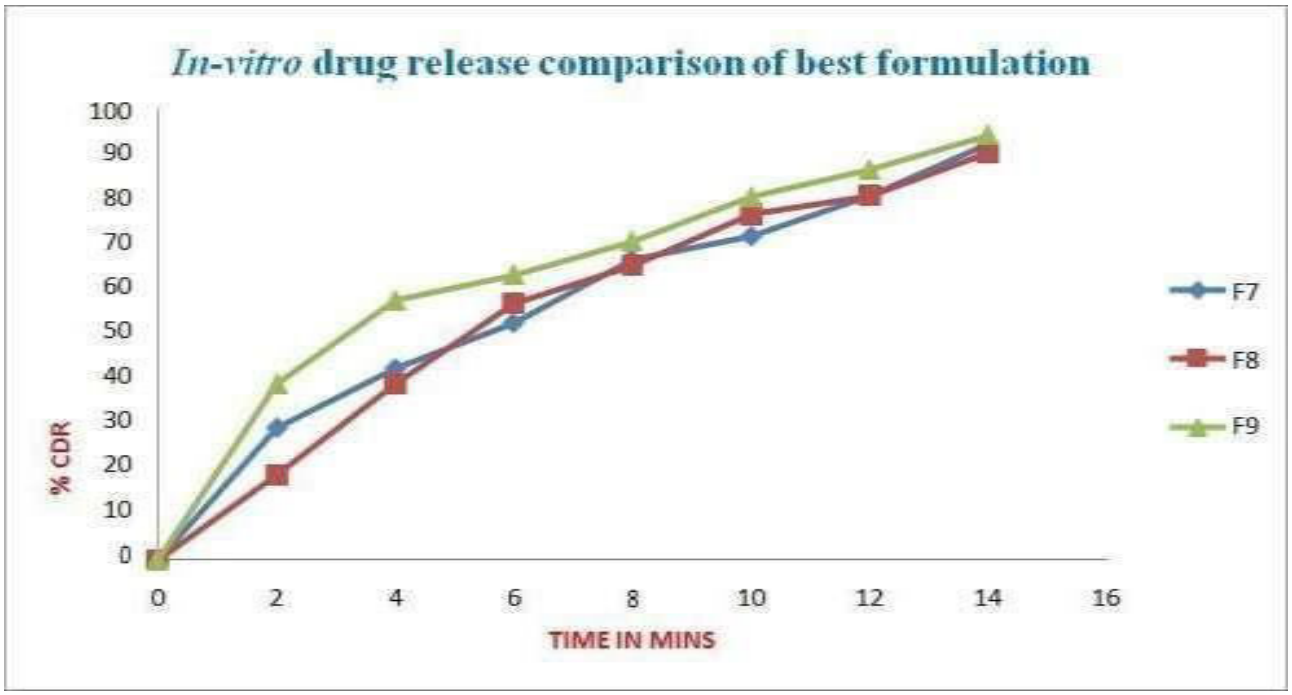


Fig.12:*F7, F8, and F9 are compared as the best formulations for in vitro drug release*.

Conclusion

The current study determined that the direct compression method was used in the production of the omeprazole sodium sublingual tablets. These tablets were then subjected to many assessment techniques. By employing FT-IR to investigate their compatibility, the drug and excipients found that there was no interaction. The pre-compression and post-compression properties of every formulation were assessed.

The outcomes showed advantageous flow characteristics.

Every formulation had a white color and a spherical morphology. The fruits tasted good, and they had no noticeable smell. Properties such as thickness, weight fluctuation, hardness, and friability of the formulations were evaluated. It was found that all of these measurements fell within ranges that were appropriate for each formulation. The range of values is 32 to 35.

According to the study's findings, every tablet that was made had good physical characteristics. In vitro research revealed that the F9 formulation, which contains the same quantities of kyrone T-314, crosspovidone, and sodium starch glycolate, showed a greater degree of drug release than the other formulations.This suggests that fragmentation is happening quickly. 94.01% of the medication was released, which was deemed satisfactory.

References

1. Kumar S, Kumar A, Gupta V, Malodia K and Rakha P. Oral Extended Release DrugDeliverySystem: APromising Approach. Asian J PharmTech. 2012;2(2):38-43.
2. RathoreAS,JatRC,SharmaNandTiwariR.AnOverview:MatrixTabletasControlled Drug Delivery System. Int J Res and Development in Pharm and Life Sci.2013;2(4):482-492.
3. Chugh I, Seth N and Rana A.C. Oral sustained release drug delivery system. Int Res JPharmacy2012;3(5):57-62.
4. Vinay K, S K Prajapati, Girish C,S, Mahendra S and Neeraj k. Sustained release matrixtypedrug delivery system. IRJP 2012;1(3):934-60.
5. Parashar T, Soniya, Singh V, Singh G, Tyagi S, Patel C and Gupta A. Novel OralSustained Release Technology: A Concise Review. Int J Res & Development in PharmandLifeSci. 2013;2(2):262-269.
9. Hemnani M, Patel U, Patel G, Daslaniya D, Shah A and Bhimani B. Matrix Tablets: AToolof ControlledDrug Delivery.American JPharmTech Res.2011;1(4):127-143.
10. DashTR,VarmaP.MatrixTablets:AnApproachTowardsOralExtentdedReleaseDrugDelivery. Int JPharma Res& Review.2013;2(2).
11. RiederA.AwarenessandcontrolofhypertensioninAustria.JHuman Hypertension 2004:535-537.
12. TaniraMOM,BalushiKA.GeneticVariationsRelatedToHypertension:AReview.JHuman Hypertension. 2005:7-19.
13. Remington'sTheScienceandPracticeofPharmacy,20th Edn.,LippincottWilliamsandWilkins,ThomasWai-Yip Leeand Joseph R.Robinson, In;Maryland. 2000: 1069-1070.
14. Harsh Mohan. The kidney and lower urinary tract. In chapter 19, Texbook of pathology:4thedition. New Delhi:JayppeBrothers MedicalPubhlishers; 2000:670-672.
15. Tripathi KD. Anti- hypertensive drugs. Essentials of medical pharmacology. 5th edition,Jayppebrothers medicalpublishers;NewDelhi.