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Development and Evaluation Orodispersible Tablets containing Taste Masked Zopiclone

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ABSTRACT

The objective of this investigation was to an orodispersible tablet containing a drug-resin combination that masks the particular bitterness of Zopiclone using polymers with low cation exchange. The resins Indion 204, Tulshion 335, and Doshion P533 were utilised. Indion 204 resins were chosen for further research due to their high capacity for drug loading. The ratio of medication to resin, resin soak time, stirring time, and pH all had a significant effect on maximal drug loading. The drug-resin combination was investigated using DSC and FIR spectroscopy. Before being turned into an orodispersible tablet, the drug-resin mixture was subjected to a variety of tests, including panel taste mask evaluation, drug content and in vitro drug release in salivary and stomach pH conditions. Finally, the evaluation criteria for orodispersible pills were examined.

Keywords: Zopiclone, Taste masking, Indion 204, Tulsion 335, Doshion P533

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INTRODUCTION

Chewable tablets, capsule suspension, lozenges, mouthwashes, dentifrices, syrups, and ingestible ointments are examples of oral pharmaceuticals with a perceived bitter taste. However, certain components, including as flavours, sweeteners, gelatin, gelatinized starch, chitosan, cyclodextrin, lecithin and lecithin-like compounds, surfactants, salts, and ion exchange resins, can be used to mask bitterness, resulting in better taste. Taste is a significant component influencing patient compliance. Unwanted taste is a significant formulation issue that many drugs experience. Administering bitter medications in a way that is acceptable to patients, particularly children, is a significant issue for healthcare workers. In fact, taste masking has emerged as a viable technique for improving patient compliance and product commercial success [1-6].

Solid, insoluble, and extremely high molecular weight, ion exchange resins matrices having pores on the surface. They are typically in the form of tiny (1-2 cm diameter) beds manufactured from an organic polymer substrate and capable of exchanging mobile ions with a charge equal to that of the surrounding media. It can be employed in pharmaceutical formulations to stabilise sensitive components, prolong the duration of drug release, dissolve tablets, and disguise flavour. Ion exchange resins are utilised for taste masking because they contain a large number of binding sites, a high capacity for drug loading, and are free of adverse local and systemic consequences. The resins can carry the medication and pass unnoticed in the salivary environment, releasing the medication. Drugs are most likely eluted from exchange resins by H+, Na+, or K+ ions, and from ion exchange resins by Cl-, as these ions are found in the highest concentrations in the secretions of the gastrointestinal tract. The rate at which ions exchange occurs is determined by solvent's and solute's permeability via the resin's pores, the number and size of which are determined by the degree of crosslinking. The length of the diffusion channel is directly proportional to the resin's particle size. [7, 8]

Bitter cationic pharmaceuticals can be adsorbed onto a weak cation exchange resin with carboxylic acid activity to produce a non-bitter compound. Indion 204 is a carboxylic acid functionalized weak acid cation exchange resin. It is built on a matrix of cross-linked divinyl benzene acrylic copolymer. It has a large capacity, is insoluble in all major solvents, and has outstanding physical, chemical, and operational properties. It is used as a taste masking agent, along with Indion 204, Tulsion-335, and Doshion P551, because it is a weak acid cation exchange resin that forms a complex with the medication that does not

release the medication into the saliva but is weak enough to be broken down by the stomach's hydrochloride acid. It is not absorbed by bodily tissues due to its enormous molecular weight, making it safe for humans. [9]

Zopiclone is a non-benzodiazepine hypnotic drug with strong sedative effects. Zopiclone has a 75-80% oral bioavailability and a biological half-life of 3.8 - 6.5 hours. Zopiclone interacts with the benzodiazepine receptor complex, facilitating the action of gamma-aminobutyric acid (GABA). It does not appear to interact with any benzodiazepine-specific receptors, but rather nearby locations on the receptor complex. GABA binding to the GABA-chloride ionophore complex is more enhanced with benzodiazepines than with zopiclone. Zopiclone has no affinity for serotonin, GABA1 and GABA2 adrenergic receptors, or dopamine receptors.[10,11,12,13]

MATERIAL AND METHOD

Cipla Limited provided Zopiclone as a free sample, whereas ion Exchange India Ltd provided Indion 204, Tulshion 335, and Doshion P533.

Method of Analysis [14,15,16]

Preparation of taste masked product and its optimization

a) Resinate preparation in a batch process:

Procedure for complexation:

Step I: Weighing the medication and resin exactly to achieve the required ratio.

Step II: A resin slurry was prepared and immersed for ten minutes in deionized water.

Step III: Deionized water was used to make the solution of medication.

Step IV: While stirring, Gradually, the medication solution was mixed into the resin solution.

Step V: There was a constant mixing of the drug resin mixtures with an emphasis on the independent variable and then subjected to UV analysis to determine drug loading.

b) Optimization Study:

i) Variable of independence

Independent variable analysis is used to determine the production of flavour masked resinate in a stepwise fashion.

1) Ratio of drug resins to be chosen

Three batches of drug–resin slurry in ratios of 1:1, 1:2, and 1:3 were prepared. For five hours, the slurry was stirred. Separation of the obtained resins was accomplished using filtration. A UV spectrophotometer with a wavelength of 303 nm was used to measure the drug loading capacity with the drug–ratio after extensive washing with deionized water. Other process parameters were optimised using the optimised drug-resin ratio.

2) The Effect of Resin Soaking Time

We evaluated the influence of resin soaking time on drug loading. For 10, 30, 40, 60, 90, and 120 minutes, a sample of resins was soaked in deionized water upto 25 ml. An carefully weighed quantity of Zopiclone (as per 1:3) was administered to previously soaked resins. The solution was stirred for 30 minutes. Filtration was performed on the mixtures, and the amount of the filtrate included unbound drugs to be determined at 303 nm.

The influence of resin stirring time on drug loading was investigated. Selected resins were soaked in 25 ml deionised water for 30 minutes. Zopiclone was carefully weighed and added to previously soaked resins in a 1:3 ratio. For 1 hour, 2 hours, 3 hours, 4 hours, and 5 hours, the solutions were stirred. Filtration was performed on the mixtures, and the amount of unbound drug in the filtrate was determined at 303 nm.

The pH Effect

We explored the influence of pH on drug loading. A precise dose of Zopiclone (in a 1:3 ratio) was administered to selected resins after 30 minutes of soaking in 25 ml of pH 1.2 to 7 solutions (made by combining normal hydrochloric acid and sodium hydroxide solutions). The solutions were stirred for 30 minutes. Filtration of the mixtures revealed an estimated unbound drug concentration of 303 nm in the filtrate.

The UV technique is used to determine the threshold bitterness concentration.

a) Determination of the pure drug's threshold bitterness concentration using the UV method:

5 mg pure medication in a tasting tube containing 15 ml phosphate buffer 6.8, and examine the concentration of pure drug after 60 seconds of manual shaking in buffer pH 6.8. A flavor-masked product was carefully weighed and put to a taste tube containing 15 ml of 6.8 phosphate buffer. Then, if the medication release concentration from resinate is less than the threshold concentration, taste masking has been successfully accomplished.

b)Study of volunteers to determine the threshold bitterness concentration of resinate:
The bitter taste threshold for zopiclone was found through an analysis of six volunteers' bitter taste judgments (three females and three males). A series of zopiclone aqueous solutions with concentrations of 0.5, 2,4,6,8, and 10 g/ml were created as standard solutions. The procedure that was followed was as follows: 1ml of each standard solution was inserted into the tongue's centre and held for 30 seconds in the mouth, and then rinsed completely with distilled water. The threshold concentration was chosen as the lowest quantity with a bitter taste among the various zopiclone concentrations.

Evaluation of taste masked products

a) Sensory Evaluation of a masked resinate with a masked taste: The flavour was reviewed by a panel of six individuals. Human tasters were asked to express their opinion on the flavour of disguised resinate.
b) The drug content of complexes was determined by immersing a weighed quantity of complex in a known volume of 0.1N HCl for 5 hours and then analysing it using a UV method set to 303 nm.
c) Differential Scanning Calorimetry Study: The DSC technique is highly useful in the development of drug-resistant compounds. Thermal examination of the samples was performed using a differential scanning calorimeter. Ten milligramme samples were placed in aluminium pans. The thermograms were acquired at a 100 degree Celsius per minute scanning rate throughout a temperature range of 40 to 3000 degrees Celsius. DSC thermograms of pure resin indion, a physical mixture of the drug and resin Indion 204 in the same ratio as in the formulation, and a thermogram of the drug-resinate complex were obtained in the current study.
d) FT-IR spectral measurements were made with a Jasco Japan 460 plus instrument, having a scanning range of 4000 to 400 cm-1.
f) Studies on dissolution:
Taste-masked evaporation *In vitro* Dissolution in 0.1N HCl: The *in vitro* release studies were carried out for one hour using the USP II paddle device. The speed of the stirring was adjusted to 50 rotations per minute. Separately, the dissolving media was produced in a pH 6.8 phosphate buffer (900ml) for taste evaluation and in 0.1 N HCl for drug release determination. 5ml samples were taken at 15-minute intervals. removed and refilled with the identical solutions. The solutions extracted from each vessel were diluted and the drug concentration in each vessel was determined spectrophotometrically at 303nm. Each scenario involved determining the percent drug release using a standard calibration curve for the medication in the same dissolving media.

Formulation of an oral dispersible tablet containing taste-masked Zopiclone granules

Formulation and assessment of a taste-masked DRC orodispersible tablet

In the preparation of orodispersible tablets (ODT) containing Indion 204, excipients included mannitol as a diluent, aspartame as an artificial sweetener, Microcrystalline Cellulose as a diluent and disintegrant, Cross povidone as a tablet disintegrant, purified talc as a glidant, and magnesium stearate as a lubricant. Table 1 shows the composition of an orodispersible tablet.

Table 1: Composition of Orodispersible tablet

Ingredients	Weight mg
Complex of Drug-resin	Equivalent to 7.5 mg of Zopiclone
d-Mannitol	138
Microcrystalline Cellulose	28.08
Cross povidone	5
Colloidal unhydrous silica	0.62
Aspartame	2.5
Purified talc	1
Magnesium stearate	1

The following ingredients were accurately weighed and sifted through screen no. 40 before being properly blended in a polybag using the tumble method: DRC, mannitol, aspartame, microcrystalline cellulose, cross povidone, and colloidal unhydrous silica. The blend's flow characteristics were evaluated.
Following flow property measurements, pure talc and magnesium stearate were carefully weighed, sifted through screen no. 40, and completely mixed with the powder blend for 2 minutes. The final blend was also tested for flow qualities like compressibility, Hausner's ratio, and angle of repose. The production procedure for the orodispersible tablets was determined using flow characteristics calculations.
The tablets were compressed at a fixed compression force using the direct compression method and a Karnavati rotating compression machine. The tablets' diameter and thickness, as well as their hardness, weight variation, *in vitro* USP disintegration, wetting time, assay, friability, and *in vitro* drug release, were all measured.

Evaluation of tablets

The tablets were evaluated for the following parameters:

General appearance:

Five tablets from each batch were chosen at random and their organoleptic qualities, such as colour, odour, taste, and form, were examined.

Thickness: Verniercalipers were used to measure the thickness of five pills. The extent to which each tablet's thickness differed from 5% of the standard value was measured. Verniercaliper was used to determine the diameter.

Hardness test:

A 'Monsanto' hardness tester was used to determine the tablets' hardness. The tester is constructed of a barrel that holds a compressible spring between two plungers. By contacting the lower plunger with the table, a zero reading is obtained. By turning a thread bolt, the upper plunger is forced against a spring, causing the tablet to break. When the spring is squeezed, a pointer in the barrel moves along a gauge, indicating the force, which is a measure of hardness.

Weight variation test:

Weighed a random sample of twenty tablets and calculated the average weight. After that, the percentage deviation from the mean was calculated. IP requires that no more than two individual weights deviate from the average weight by more than the amount specified in table no.4, and no more than double that percentage.

Table 2: IP standard of % of weight variation

Average weight of tablet	% deviation
80 mg or less	10
More than 60 mg but less than 250 mg	7.5
250 mg or more	5

Because the average weight of the tablets manufactured is in the range of 180-210 mg, the limit of percent deviation to be taken is 7.5.

Friability test:

This experiment made use of a Roche friabilator. A plastic chamber was rotated at a pace of 25 revolutions per minute and the tablets were dropped from a distance of six inches with each revolution, causing abrasion and shock. The friabilator is typically set to 100 revolutions for a batch of ten pre-weighed tablets. To re-weigh the tablets, they are ground up and powdered.

Weight loss of less than one percent is deemed acceptable for compressed pills.

***In vitro* disintegration test:**

If the tablet is to be used as a dispersible tablet, this test is performed to ensure that it disintegrates in water. One tablet is placed into one tube of disintegration apparatus IP. In addition, a disc is inserted inside the tube. The assembly is suspended in distilled water in a beaker, and the system is run until the tablet disintegrates. Dispersible tablets must disintegrate within 3 minutes when tested using the tablet disintegration test to be in accordance with the IP standard.

***In vitro* dispersion time (with simulated salivary fluid)**

If the tablet is to be used as an Orodispersible tablet, this test is performed to ensure that it disintegrates in the salivary fluid. Dropping a pill into a measuring cylinder holding 6 ml of synthetic salivary fluid of 6.8 resulted in an *in vitro* dispersion time of 6.8. Three tablets were chosen at random from each formulation, and *in vitro* dispersion time was measured.

Simulated salivary fluid preparation:

pH 6.8 phosphate buffer simulates salivary fluid. In 1000ml of water, dissolve 13.872g of potassium dihydrogen phosphate and 35.084g of disodium hydrogen phosphate.

Wetting time:

Wetting time is the amount of time it takes for a tablet to disintegrate while it is kept immobile on tissue paper in a Petri dish. Because the pill is immobile on the tongue, this procedure will replicate in-vivo breakdown. The time required for complete wetting was determined by placing a tablet on a folded piece of tissue paper and inserting it into a small petri dish containing 6 ml of simulated saliva pH 6.8. Five tablets from each batch were utilised to compare the outcomes to a commercial product.

***In vitro* Dissolution study:**

A dissolution test equipment with a paddle speed of 50 rpm was used to investigate the dissolution profile of Zopiclone tablets. In 7.4 ph Phosphate buffer, dissolution was evaluated. Dissolution was carried out in 900ml of water at 370.5 0 C. The drug solution absorbance was measured at 303nm in 1 cm cuvettes using a uv-visible spectrophotometer at 5, 10, 15, 20, and 60 minute intervals. Aliquots were drawn at 5, 10, 15, 20, and 60 minute intervals and filtered using Whatmann filter paper.

RESULT AND DISCUSSION

Preparation of taste masked products:

Preparation of taste masked drug resin complexes by batch method using ion exchange resin.

Selection of resin:

The selection of resin for a certain application necessitates consideration of a number of criteria. Cationic and anionic exchange resins are utilised depending on the acidic and basic properties of the medicines. Anion exchange resins are utilised for acidic drugs, and cationic exchange resins are used for basic drugs. In the current study, a weak cationic exchange resin, i.e. Zopiclone flavour masking agents included Indion 204, Tulsion 335, and DoshionP533. Because of the limited binding capacity and basic nature of Zopiclone, weak cationic exchange resins were chosen for the quick release taste masking formulation. Initial formulation testing demonstrated that stirring speed, drug: resin ratio, pH effect, and stirring time had a significant impact on free drug concentration, formulation of tasteless drug-resin complex, and formulation drug loading efficiency. As a result, these characteristics were investigated in order to optimise the formulation. The drug: resin ratios were varied between 1:1 and 1:3. Table 3 shows the outcomes of optimization studies.

Table 3: Selection of Drug resin Complex

Sr. No.	Resin	Batch	Drug: resin ratio	Taste	Drug loading
1	Indion 204	F1	1:1	+	52.49
2		F2	1:2	++	72.95
3		F3	1:3	+++	85.60
4		F4	1:4	+++	86.13
5	Tulsion 335	F5	1:1	+	45.00
6		F6	1:2	+	49.32
7		F7	1:3	++	63.41
8	Doshion P551	F8	1:1	+	51.37
9		F9	1:2	+	62.45
10		F10	1:3	++	78.12

+ Slightly taste masking, ++ moderate taste masking, +++ Complete taste masking

Various drug resinate complexes were produced using a batch approach with varied ratios of ion exchange resins. Batch F3, containing Indion 204 in a 1:3 ratio, was chosen based on flavour masking and percent drug loading efficiency. The batch F3 features perfect flavour masking and a medication loading of 85.60 percent. Batch F4 likewise demonstrated good taste masking with percent drug loading, however there was no significant change when compared to Batch F3, hence the Batch F3 drug resin Complex was chosen for further research.

Effect of soaking time

The effect of resin soaking time on drug loading revealed that the percentage of drug bound to resin rose as resin soaking time increased, as indicated in Table 4. From 30 to 120 minutes, the percentage of medication bound to resin increased somewhat. As a result, a soaking duration of 30 minutes was chosen for future investigation.

Table 4: Effect of soaking time on drug loading

Drug: resin	Soaking time (min)	% Drug loading
1:3	10	78.16
	30	87.12
	40	87.2
	60	88.56
	90	88.88

Effect of stirring time

The effect of stirring time on drug loading revealed that as the stirring time rose, the proportion of drug bound to resin increased, as indicated in Table 5. From 30 minutes to 6 hours, the percentage of medication bound to resin increased somewhat. As a result, a stirring time of 5 hours was chosen for further investigation.

Table 5: Effect of stirring time on drug loading

Drug: resin	Soaking time (min)	Soaking time	Indion 234
1:3	30	30min	65.12
		1hr	67.74
		2 hr	73.34
		3 hr	75.34
		4 hr	85.11
		5 hr	91.52
		6 hr	88.34

Effect of pH

The effect of pH on drug loading revealed that when the pH declined, the percentage of drug bound to resin reduced, as indicated in Table 6. The highest loading was achieved between pH 4–5.

The UV technique was used to determine the threshold bitterness concentration

Determination of the Bitterness Concentration Threshold UV Method, which is used for taste analysis by U.V. The pure drug release concentration was reported to be 20 g/ml after 60 seconds of manual shaking in buffer pH 6.8. and the drug release concentration from resinate was found to be 12g/ml. After shaking, the drug's flavour has been successfully concealed.

Table 6: Effect of pH on drug loading

Drug: resin	Soaking time(min)	Stirring Time	pH	Percentage of drug bound to resin (Indion 204)
1:3	30	5hr	1	71.06
			2	73.99
			3	81.44
			4	85.13
			5	91.65
			6	90.05
			7	88.78

The research of volunteers to determine the threshold bitterness concentration of resinate

Volunteers' study determined the drug's bitterness threshold. The response of participants to different concentrations of Zopiclone was examined, and it was discovered that with the concentration of 10 g/ml, all of the volunteers felt bitterness after 30 seconds. Two respondents reported an 8g/ml bitter taste, whereas the remaining five volunteers reported a 10g/ml harsh taste. As a result, it was determined that the Zopiclone concentration threshold was 10 g/ml (Table 7).

Table 7: Determination of threshold Bitterness concentration

No. of Volunteers code	Concentration of Drug (µg/ml)					
	0.5	2	4	6	8	10
A	1	1	1	1	2	2
B	1	1	1	2	1	2
C	1	1	1	1	1	2
D	1	1	1	1	2	2
E	1	1	1	1	1	2
F	1	1	1	1	1	2

Scale: 1 = Slightly bitter, 2=Bitter, 3 = Very Bitter

Micromeritic properties of taste masked products:

The micromeritic properties of the taste-masked product, such as bulk density, angle of repose, and resinate compressibility, were found to be satisfactory.

Table 8: Micromeritic Properties of taste masked product

Sr. No.	Property	Observation
1	Bulk Density	0.54 gm/ml
2	Tap Density	0.62gm/ml
3	Angle of repose	27.24
4	Carr's index	12.90 %

Evaluation of taste masked product:

Sensory Evaluation of the Flavor-masked Resinate: When the taste-masked resinate was examined on human volunteers, the volunteers reported experiencing no bitter taste after 30 seconds, indicating that the bitter taste of zopiclone had been satisfactorily masked. Six participants rated the resinate on a scale of 0 (excellent), 1 (tasteless), 2 (somewhat bitter), 3 (bitter), and 4 (bitter) (very bitter). The subjects

attested to the success of the taste masking, as the pure medicine is significantly more bitter than the resinate. The volunteers' scale markings verified this.

Table 9: Sensory evaluation of taste masked resonates

Sr.No	Volunteers code	Mark rating to preparation	
		Drug Substance	Taste masked Resinate
1	A	4	1
2	B	4	0
3	C	4	1
4	D	4	0
5	E	4	0
6	F	4	0

Scale 0= good,1=Tasteless, 2=Slightly Bitter ,3 Bitter, 4=very Bitter.

Determination of drug content in complexes.

Using 1N HCl as a blank, the drug concentration was measured spectrophotometrically at 303nm. Drug content of the complexes produced with DRC ion exchange resin was determined to be 95.45 percent.

DSC Analysis.

Figures 1,2,3,4 show the DSC results. DSC of pure drug reveals a pronounced endothermic peak at 177^{0}C. DSC of pure resin (Indion 204) exhibits a broad endothermic peak at 223^{0}C. DSC of drug and resin physical combination reveals two independent endothermic peaks at 173^{0}C and 213^{0}C. DSC of drug-resin complex displays a broad endothermic peak from 160^{0}C to 260^{0}C, indicating drug resin complex production. The absence of a marked endothermic peak of the drug at 178^{0}C also suggests the creation of a drug resin complex.

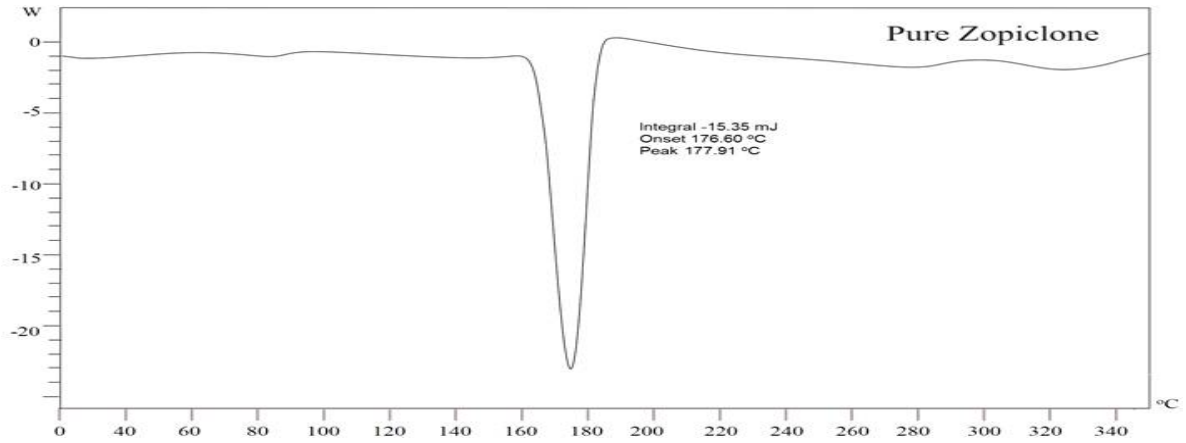

Figure 1: DSC of Pure Drug

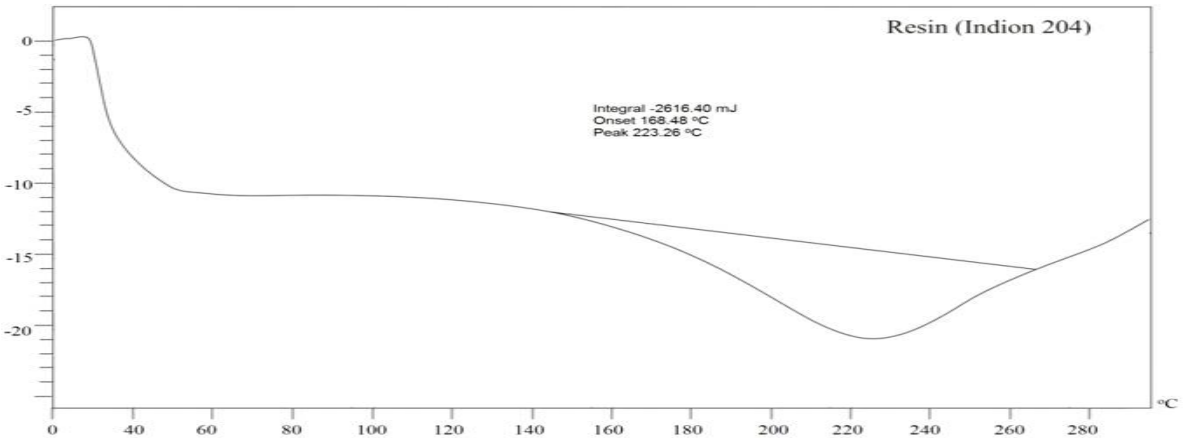

Figure 2: DSC of Pure resin (Indion 204)

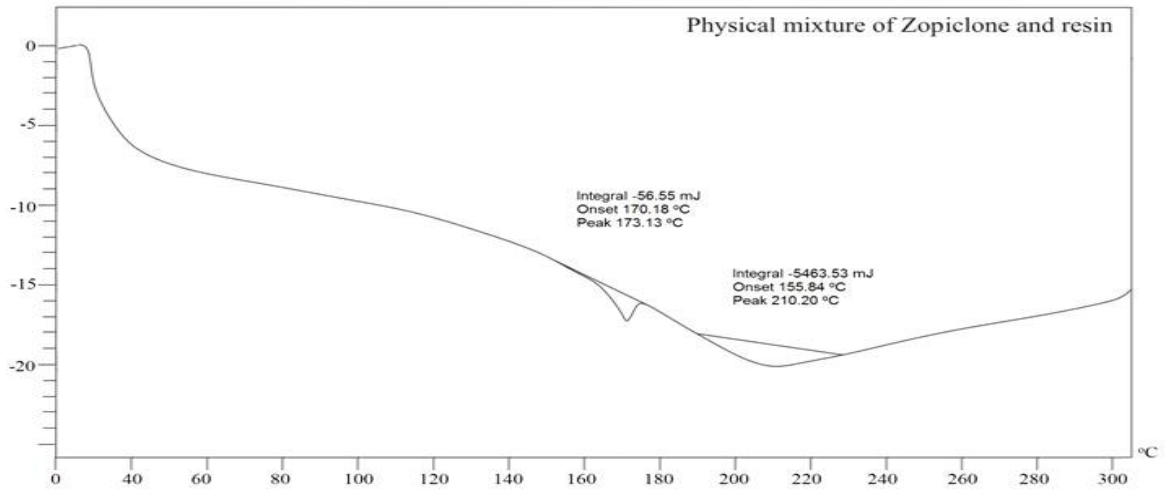

Figure 3: DSC of Physical mixture of Zopiclone and Resin

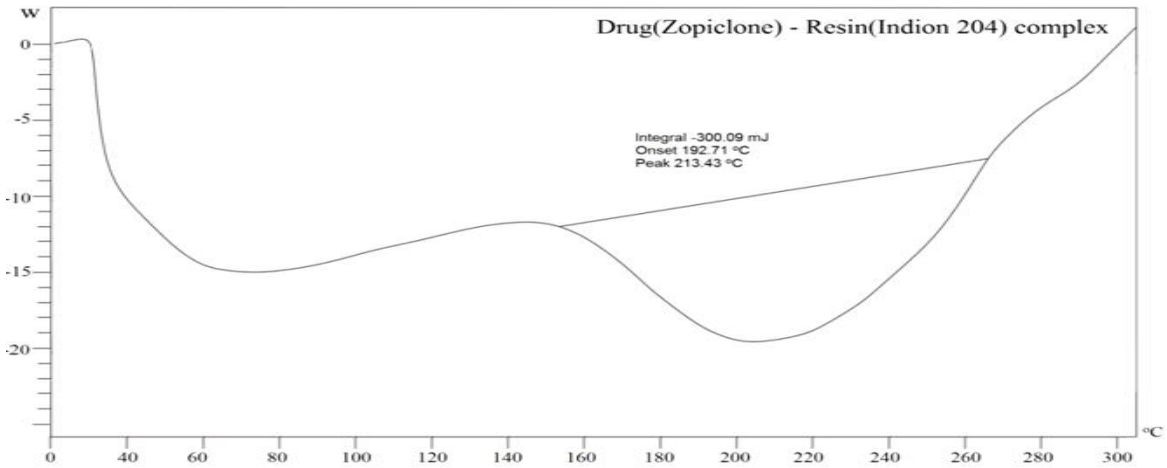

Figure 4: DSC of Drug -Resin complex

Fourier Transform Infrared Spectroscopy

IR tests on Indion 204, Zopiclone, and Resinate Complex verified complexation.

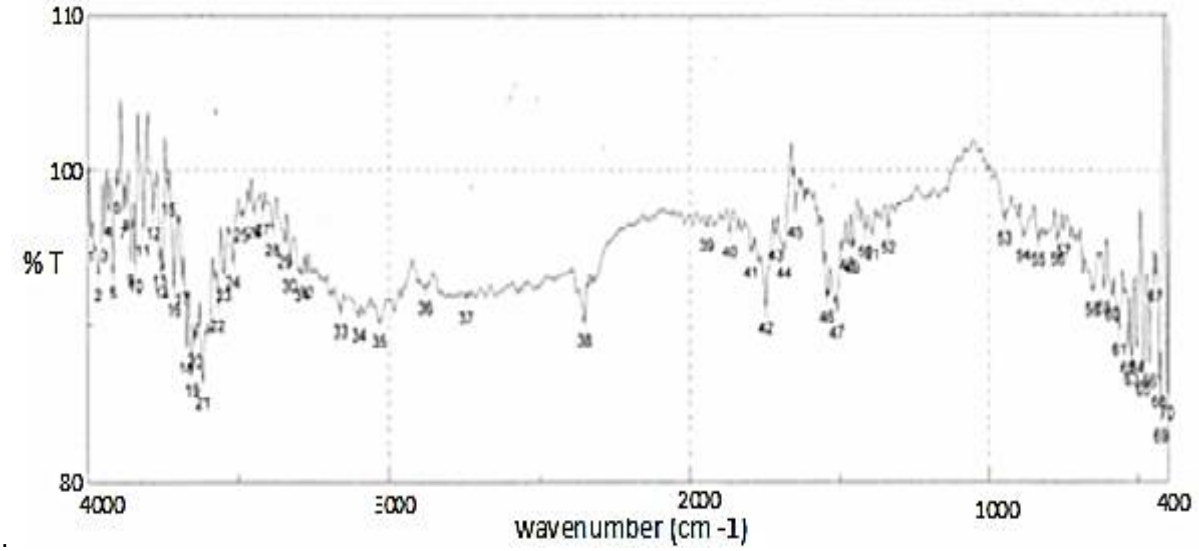

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Fig 5 IR spectrum of Indion 204

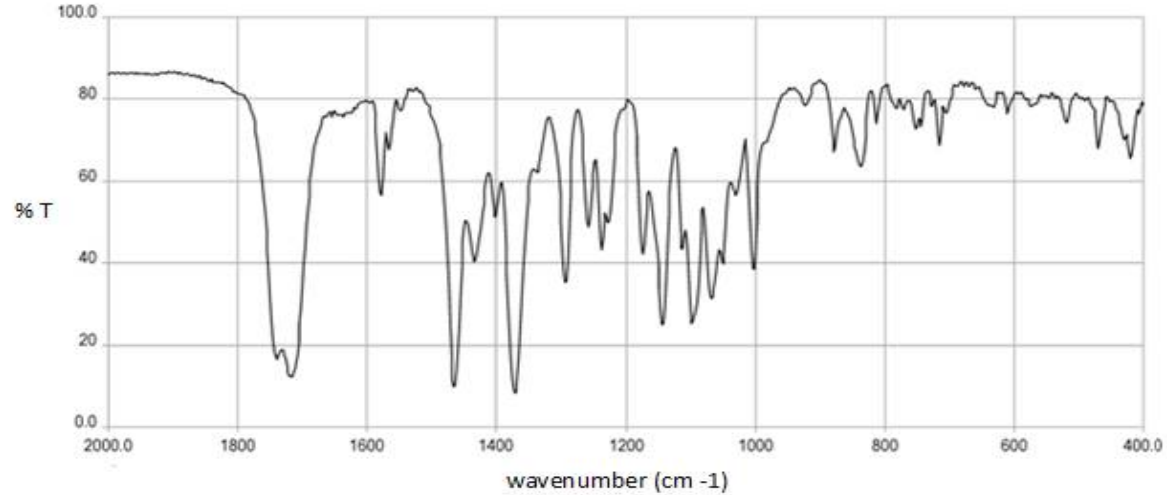

Fig 6 IR spectrum of Zopiclone

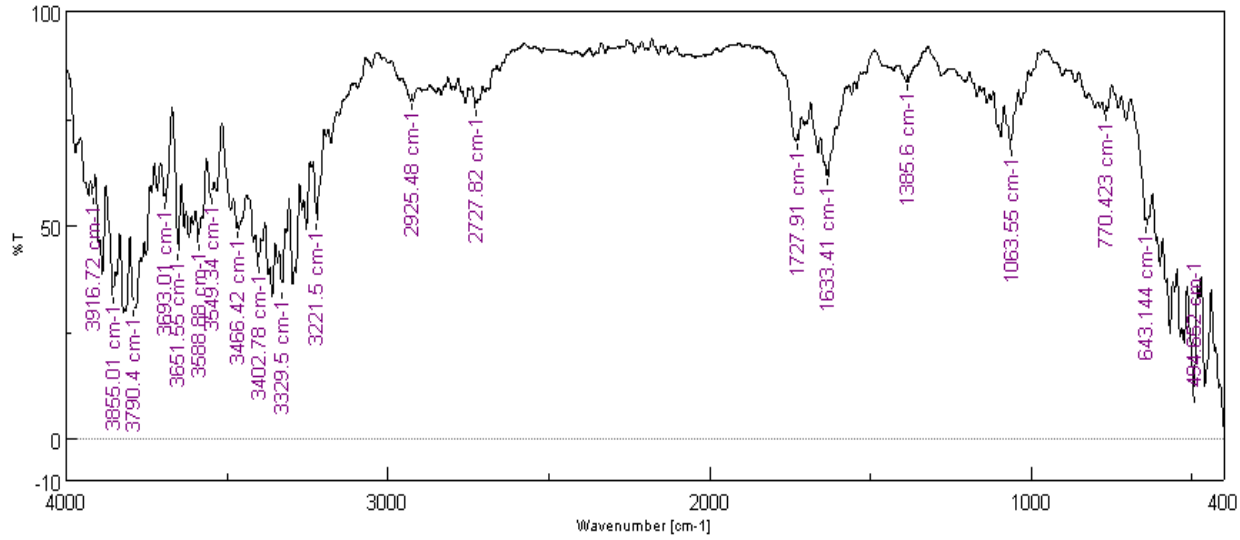

Fig 7. IR spectra of Zopiclone:Indion 204 resinate complex

Dissolution studies.

Taste was concealed by *in vitro* dissolution. Resinate in 0.1 N hydrochloric acid Figure 8 depicts the results of an *in vitro* dissolution investigation in 0.1 N HCl. As a consequence of the foregoing results, it was determined that drug release from resinate exceeded 86 percent after 1 hour, indicating that the resinate is suitable for tablet formation.

Table 10*: In vitro* dissolution of taste masked resinate in 0.1 N HCl

Time (min) (minutes)	Absorbance ± SD	Concentration Abs x K =B	Conc. C x D.F in (µ/ml)	Amount in vessel (mg) A x 900/1000	Percent drug released (%)
5	0.1503	2.03	20.3	18.3	60.6
10	0.1630	2.18	21.8	19.5	65.0
15	0.1690	2.25	22.5	20.4	68.0
20	0.1820	2.46	24.6	21.3	73.0
25	0.1875	2.41	24.1	22.0	75.3
30	0.1905	2.53	25.3	23.1	76.6
40	0.1994	2.61	26.1	23.54	78.6
50	0.2015	2.63	26.3	23.84	79.5
60	0.2187	2.86	28.6	25.82	86.0

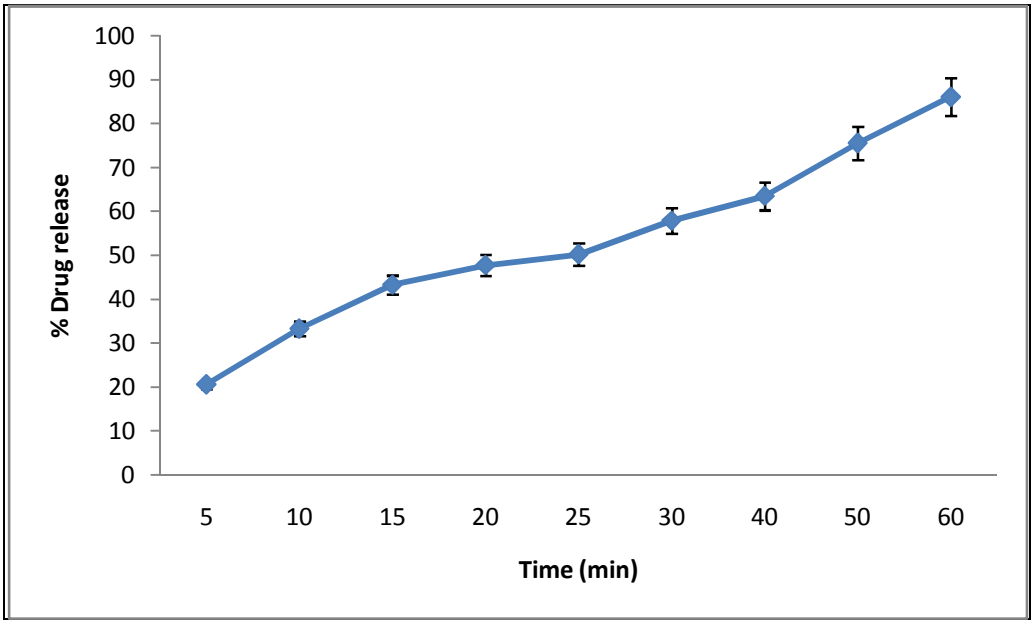

Figure 8: *In vitro* Drug release of Drug resinate in 0.1N HCl

As a consequence of the foregoing results, it was determined that drug release from resinate exceeded 86 percent after 1 hour, indicating that the resinate is suitable for tablet formation.

Drug release in Phosphate Buffer pH 6.8

The *in vitro* dissolution study in phosphate buffer pH 6.8 was performed and reported as in figure 9.

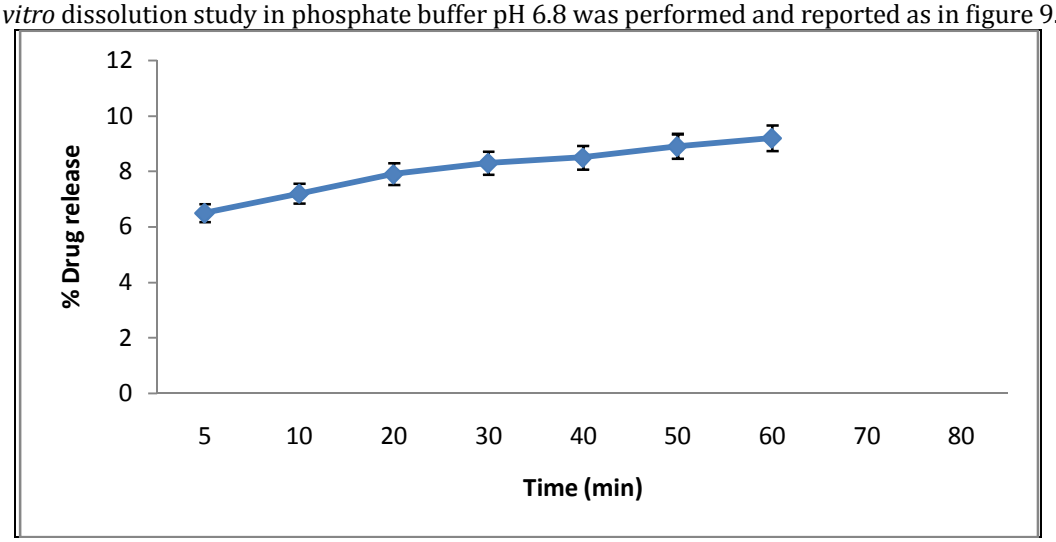

Figure 9: *In vitro* drug release of drug resinate in phosphate buffer pH 6.8

The given result confirms that drug release from resinate is less than 10% after 5 minutes, indicating that the results are suitable for taste-masked tablet formulations. Drug release is less than 10% at the end of 5 minutes in phosphate buffer pH 6.8, indicating that taste masking occurs.

Tablet evaluation:

Result of evaluation of tablet for various parameters are shown as follows:

Physical properties of the tablet.

The dimensions determined for formulated tablets were tabulated in the table 11.

Table 11: The dimensions determined for formulation tablet were tabulated

Diameter *(mm)	Thickness *(mm)	Hardness* Kg/sq.cm
12.13	3.68	2

*Each value is an average of five determinations

The tablets diameter was almost uniform in the formulas and thickness range were extremely close to within 5% of the standard value. The average hardness of the tablets was determined to be 2 Kg/sq.cm.

This guarantees that the formulations have good handling properties. The formulas and thickness range were extremely close to within 5% of the standard value. The average hardness of the tablets was determined to be 2 Kg/sq.cm. This guarantees that the formulations have good handling properties.

Weight variation test.

Table 12: Percentage weight variation

Sr. No.	Individual weight of the tablets in mg
1	194.00
2	191.10
3	193.02
4	194.10
5	191.23
6	191.56
7	193.14
8	194.12
9	192.87
10	193.31

Friability test.

$$\% \text{ Friability} = \frac{\text{Initial weight of the tablets}}{\text{Final Weight of tablets}} \times 100$$

The % friability was less than 1%, ensuring that the tablets were mechanically stable.

Results of *in vitro* disintegration time, *in vivo* Dispersion time, wetting time

Results of *in vitro* disintegration time, *in vivo* Dispersion time, *in vivo* disintegration time, wetting time are tabulated in table 13.

Table 13: Comparison of disintegration properties

Formulation parameter	Tablet Result
In vitro disintegration time *(with water)	23 sec
In vitro dispersion time* (with simulated salivary fluid)	22sec
Wetting time*	10±1.5 sec

Dissolution study:

The *in vitro* dissolution study was carried out and reported in figure 10. From the above result it was confirmed that drug release from resinate was found more than 90% at the end of 30 min.

Time (Min)	% Drug Release
0	00
5	28.3
10	48.82
15	62.46
20	75.17
25	84.6
30	96.86

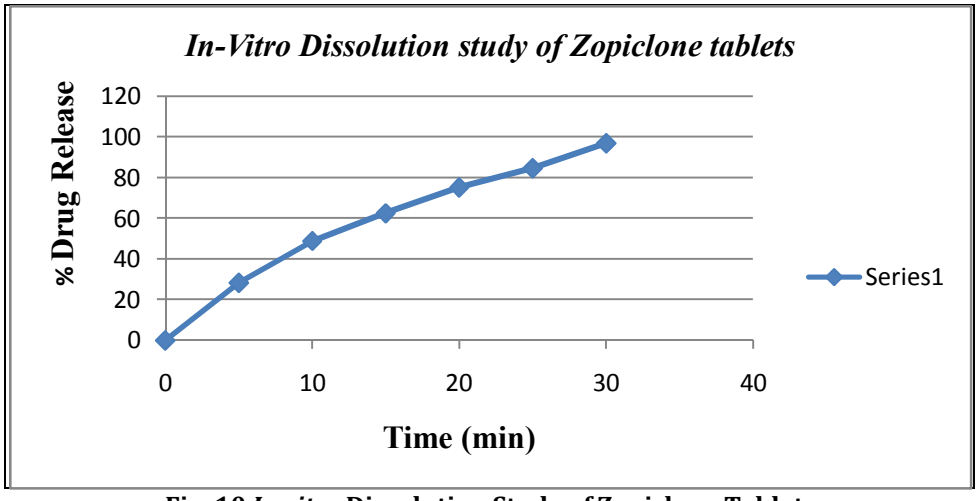

Fig. 10 *In vitro* Dissolution Study of Zopiclone Tablets

CONCLUSION

In the current study, an attempt was made to investigate the usage of ion exchange resins as taste masking agents and super disintegrates in the formulation of oro-dispersible Zopiclone tablets.

As ion exchange resins, indion 204 was employed. They were combined with the drug in various drug to resin ratios and periods and analysed for the level of complexation. The results showed that an Indion 204 drug to resin ratio of 1:3 provided the greatest amount of complexation after 5 hours of mixing.

These drug-resinate combinations were subsequently transformed into granules, which had acceptable angles of repose and bulk density values. Estimated drug content revealed that more than 90% of the drug was present. The appropriate amount of drug-resinate was taken for compression based on the drug content. The tablets were made using the direct compression approach. The samples were then subjected to evaluation studies for factors such as general appearance, thickness, weight variation, friability, and disintegration tests. The disintegration tests performed on these products revealed that the tablets disintegrate quickly, requiring 23 seconds. Dissolution experiments revealed a drug release rate of up to 95% in 1 hour.

As a result, we may conclude that weak cation exchange resins, such as Indion 204, have been shown to be effective as taste masking and super dissolving agents. As a result, we are able to meet our goals of producing oro-dispersible Zopiclone tablets with few excipients and a straightforward manufacturing procedure.

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