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Research Article

DEVELOPMENT AND CHARACTERIZATION OF TASTE MASKED MOUTH DISSOLVING TABLETS OF ZOLPIDEM TARTRATE

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ABSTRACT
The present investigation was undertaken to design a simple, rapid, cost effective and highly efficient process to fabricate a tasteless complex of zolpidem tartrate using ion exchange resin (IER), evaluate the molecular properties of the resinate and finally incorporate it into orally disintegrating tablets (ODT). The resinate formation using tulsion-335, was confirmed using the characterization methods: Fourier Transform-Infra Ray (FTIR), X-Ray Diffraction (XRD) and Differential Scanning Calorimetry (DSC). The maximum drug loading efficiency achieved was in 1:3 (drug: resin weight) ratio at pH 6.8 in a period of 4.0 hrs using methanol: water as the complexation medium. The drug release from the complex was about 0.05 mg in 60 sec in 5 ml of pH 6.8 Sorenson's buffer which has been used to mimic the salivary fluid volume and pH. The complex was compressed into mouth dissolving tablet. Dissolution studies for tablets carried out using 900 ml of Sorenson's buffer pH 6.8 at 50rpm in USP Apparatus II showed 98% or drug release in 5mins, indicating complete drug release from the complex. Resinate was tasteless and hence the fabricated ODTs would also be pleasantly tasting without any bitterness.

KEYWORDS: Zolpidem tartrate; ion exchange resin; resinate; bitter taste; orally disintegrating tablets.

INTRODUCTION

Taste of a pharmaceutical product is an important parameter for governing patient compliance. More than 50 percent of pharmaceutical products are administered orally and undesirable taste is one of the important formulation problem encountered with oral products. Thus, taste masking of oral pharmaceuticals has become an important tool to improve patient compliance and the quality of treatment especially in pediatrics.[1, 2] The masking of unpleasant taste in orally-disintegrating tablets and chewable tablets is therefore an important consideration in the formulation of many therapeutic agents and is achieved by minimizing direct contact between the active species and the taste receptors in the buccal cavity of the subject. In order to improve the palatability of a pharmaceutical product, many techniques have been developed which have not only improved the taste, but also the stability of the drug in the formulation and performance of the product. Use of Ion exchange resins is one of the methods for taste masking.

Ion Exchange Resins (IERs) For Taste Masking: IERs are high molecular weight polymers which involve the reversible interchange of ions (of like charge) between a liquid and a solid phase, with no radical change in the structure and properties of the solid.[3] They have wide applications in enhancing the stability of sensitive drugs, sustaining the release of drug, [4] as disintegrating agents and for masking the bitter taste of drug. Drug binding to the resin can be achieved by two processes. First approach is repeated elution of drug solution through a column of swollen activated resin bead where drug is allowed to

interact with binding sites of resin and second is by prolonged contact of resin with the drug solution.[5-8] Drug molecules get adsorbed on the IER, resulting in the formation of an insoluble adsorbate or resinate by forming weak ionic bonds which does not dissociate under the salivary pH conditions, hence, mask the unpleasant taste of drugs. After administration of resinate, the release of drug from the resin depends on the properties of the resin and the ionic environment within the gastrointestinal tract (GIT). Drug molecules get released from resin by exchanging with appropriately charged ions in the GIT and free drug is available for absorption.[9] The IER devoid of drug is eliminated or biodegraded from or at the site of delivery.[10]

Zolpidem tartrate is a potent hypnotic, used in treatment of insomnia as well as some brain disorders. It is a very bitter drug and has very less solublility.[11-12] The main objective of the present work is to formulate taste masked mouth dissolving tablets of an intensely bitter tasting hypnotic drug zolpidem tartrate (ZMT) using a simple, rapid and cost effective process for improved patient compliance. The bitterless complex was prepared by using Ion Exchange Resin (IER)-Tulsion 335 and molecular properties of resinate produced for taste making purpose was evaluated using XRD, FTIR and DSC. The taste masked resinate was further formulated into the mouth dissolving tablet by direct compression method using crosscarmellose sodium (Ac-Di-Sol), Sodium starch glycolate (SSG) and crospovidone as the superdisintegrants.

MATERIALS AND METHOD

Zolpidem tartrate was obtained as a gift sample from Symbiosis Pharmaceutical Pvt Ltd. Baddi. Tulsion 335 was procured from Thermax Ltd. Pune, India. Lactopress (lactose monohydrate), Avicel PH 102 (Microcrystalline cellulose), Crospovidone, Sodium starch glycolate and Ac-Di-Sol were obtained as a gift sample from Signet Chemicals (Mumbai). Sucrose, Magnesium stearate and Talc were purchased from S. D. Fine Chemicals Ltd. (Mumbai). All other reagents and solvents used were of analytical grade. Deionized water was freshly prepared whenever in use.

Activation of Resin

Batch method was used to prepare drug resin complex. Ion exchange resin Tulsion-335 was swelled with deionised water for an hour and then washed with 1N hydrochloric acid and 1N sodium hydroxide in order to remove impurities (alkali and acidic impurities). The treated resin was washed several times with freshly prepared deionized water to remove the traces of acid or alkali. This treated resin was kept in oven for 12 h at 50^0C. The dried activated resin was kept in desiccator until in use.

Effect of Drug Resin Ratio on Drug Loading

Accurately weighed 100, 200, 300, 400 mg of pretreated resin was placed in a series of 100ml volumetric flasks containing 100 mL of deionized water and was allowed to swell for 45 minutes. 100 mg of zolpidem tartrate was accurately weighed and was added to all the flasks, to obtain 1:1, 1:2, 1:3, and 1:4, drug: resin ratio and was stirred for 4hrs on a mechanical shaker to allow maximum possible loading. 5 ml of methanol was added to dissolve unloaded drug, the mixture was filtered immediately by vacuum filtration and the residue was washed with 200 mL of deionized water. Finally, the unbound drug in filtrate was estimated by UV Spectrophotometry at 295 nm and drug-loading efficiency was calculated. The prepared resinate was dried in vacuum oven at 60ºC till the moisture contents was below 5%.

Effect of Concentration of Resin on Drug Loading

For optimizing drug:resin ratio, Accurately weighed quantity of zolpidem tartrate (100 mg) was added to each of the four beakers containing 100, 200, 300 and 400 mg of Tulsion 335 swelled in 100 ml of deionized water. The mixture was stirred for an hour. Drug resin complex was collected by filtration, washed with 50 ml of deionized water and percentage of drug adsorbed onto each resin was determined.

Effect on Swelling of Ion Exchange Resin by Stirring Speed and Time

To optimize the effect of swelling of ion exchange resin on drug loading, accurately weighed activated resin was stirred at 50 and 100 rpm for different time period (15, 30, 60 min) in 100 ml deionised water. After specified time, the drug (100 mg) was added, stirred for 4 h and filtered. It was then subjected to

UV spectroscopy at 295 nm to determine the amount of drug loaded and then percentage of drug loaded was calculated.

Effect of Complexation Time on Drug Loading

To optimize the effect of complexation time on drug loading, accurately weighed zolpidem tartrate (100 mg) was added to 300 mg of tulsion 335 solution and slurred in 100 ml of deionized water in beaker. Five batches with stirring time of 1, 2, 3, 4, 5 h were processed for resin. The mixtures were filtered and subjected to UV spectroscopy at 295 nm to determine the amount of drug bound. Then percentage drug loading was calculated.

Effect of pH on Drug Loading

Zolpidem Tartrate (100 mg) was added to Tulsion 335 (300 mg) in beaker containing 100 ml of different pH solutions. The pH was adjusted using standard solutions of hydrochloric acid and sodium hydroxide, stirred for 4 h. The mixtures were filtered and subjected to UV spectroscopy at 295 nm to determine the amount of drug complexed.

Evaluation of Molecular Properties of Drug Resin Complex

Thermal analysis[13]

Thermal analysis was carried out with the help of DSC equipment using indium as a standard with a melting point of 156.63°C and calibration energy of 28.89 J/g. The temperature was increased from 25°C to 300°C at a heating rate of 10°C/min under a flow of nitrogen (80 mL/min). From each stressed sample approximately 5 mg of the sample of resin, drug and resinate was weighed and subjected to DSC.

X-ray diffractometry

The Powder XRD patterns of Zolpidem Tartrate, Tulsion-335 and Zolpidem tartrate resinate were recorded .Samples were irradiated with monochromatized Cu Ká radiation (1.5406 Å) after passing through Nickel filters and were analyzed between 40° and 2° (2è) with scan step size 0.0167 in spinning condition and number of scan steps was 2274. The voltage and current applied were 45 KV and 40 mA, respectively.

Fourier-transform infrared spectrophotometry

Infrared spectra of Zolpidem Tartrate, Tulsion-335 and Zolpidem resinate were obtained using FTIR spectrophotometer. The pellets were prepared on Potassium bromide press, and the spectra were recorded over the wave number 4000 to 400 cm^{-1}.

Determination of *in vitro* drug release

The release of drug from resinate was carried out from USP dissolution apparatus II. Three different dissolution media (900 mL) used were Sorenson's Buffer (pH 6.8), 0.1N HCl (pH 1.2) and Phospahte Buffer (pH 7.4) at 37 ± 1^0C. Rotation speed was 50 rpm. An accurate weight of resinate equal to 5mg of zolpidem was added in dissolution media. Aliquots of 5 mL was collected and replaced with fresh medium at 5 minutes. After filtration and appropriate dilution absorbance of collected sample was measured by UV-VIS spectrophotometer at 295 nm.

I*n vivo* taste evaluation

Taste evaluation of the drug resin complex was performed by panel of six healthy volunteers in the age groups of 25 to 30 years. The 5 mg equivalent to Zolpidem tartrate and Zolpidem tartrate resinate were held in mouth for 60s by each volunteer, and the bitterness level was recorded using a numerical scale. After 60 s, complex was spitted out and the mouth was rinsed thoroughly with mineral water.

Preparation of Zolpidem Tartrate Mouth Dissolving Tablets

Mouth dissolving tablets of zolpidem tartrate were prepared using superdisintegrants. The critical parameters to formulate a mouth dissolving tablet are the choice of superdisintegrant and optimization of concentration of superdisintegrant. The mouth dissolving tablets of Zolpidem Tartrate were prepared by using superdisintegrants in different ratios as shown in table 6. The ingredients were mixed homogenously and co-grounded in a glass mortar and pestle (except talc and magnesium stearate). Finally talc and magnesium stearate were added and mixed for 5 minutes.

Evaluation of Tablet Blend

The characterization of mixed blend done for the flow property of powder that are Micromeritic properties (Bulk density and tapped density) were determined using a bulk density apparatus and Flow properties **(**Angle of repose, compressibility index and Hausner ratio) were evaluated as per methods described in USP.

Compression of Tablets

The mixed blends of excipients were compressed using a single punch tablet punching machine (Cadmach, Ahmedabad) to produce flat faced tablets weighing 100 mg each with 7 mm diameter. A minimum of 100 tablets were prepared for each batch.

Evaluation of Mouth Dissolving Tablets

Tablets were evaluated for diameter, thickness, weight variation, hardness test, friability, drug content uniformity as per the USP method of tablet evaluation. As per the European Pharmacopoeia the Mouth dissolving tablets should disintegrate within 3mins.

Dissolution Test & Drug Content Uniformity

In Vitro dissolution studies for all the fabricated tablets was carried out using USP apparatus II at 50 rpm in 900 ml of Sorenson's buffer (pH 6.8) as dissolution media, maintained at 37±0.5^{o}. 5 ml aliquot was withdrawn at the specified time intervals, filtered through whatmann filter paper and assayed spectorphotometrically at 295 nm. An equal volume of fresh medium, which was prewarmed at 37^{o}C was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test. The various kinetic treatments were given to the dissolution data. The *in vitro* permeation data obtained were subjected to a zero order and first order kinetics to understand the release profile and release mechanism.

For drug content uniformity, ten randomly selected tablets were weighed and average weight was calculated, the tablets were powdered in a glass mortar pestle. The weight equivalent to 5 mg zolpidem tartrate was weighed. The weighed amount was dissolved in 5 ml of methanol in separate volumetric flask using magnetic stirrer, the volume was adjusted to 100 ml, with Sorenson's buffer (pH 6.8) and the solution was filtered. An aliquot of 1.0 ml from these solutions was diluted to 10 ml Sorenson's buffer (pH 6.8) in separate volumetric flask. The content in each formulation was determined spectrophotometrically at 295 nm.

Stability Study

The Mouth Dissolving Tablets of Zolpidem Tartrate were packed in wide mouth air tight glass container and stored under the following conditions for a period of 7 weeks:

■30 ± 1^{o}C ■40 ± 1^{o}C and 75 ± 5% RH ■50 ± 1^{o}C

The tablets were withdrawn after every week and analyzed for physical characterization and drug content spectrophotometrically at 295 nm.

Comparison of Release with Marketed Tablets

Dissolution rate study was conducted for conventional marketed tablet. The various kinetic treatments were applied to the dissolution data. The *in vitro* permeation data obtained were subjected to find the release profile and release mechanism and to compare it with the optimized FDT formulation (FDT2) as shown in figure 5.

RESULTS

Effect of Concentration of Resin on Drug Loading

Batches were fabricated with different ratios of drug to resin (w/w) ranging from 1:1 to 1:4 and it was observed that there was a sharp increase in loading efficiency with increase in the ratio from 1:1 to 1:3. Increase in ratio from1:3 to 1:4 showed no significant increase in the loading. The data is reported in Table 1

Effect on Swelling of Ion Exchange Resin by Stirring Speed and Time

The resin requires proper swelling time for maximum drug loading. It was concluded that a swelling time of 60 minutes was sufficient for maximum swelling of ion exchange resin. The data is reported in Table 2.

Effect of Complexation Time on Drug Loading

The effect of complexation time on drug loading it was found that with increase in time for stirring the solution, the drug loading gets increased and maximum drug loading was achieved at 4 h. The data is reported in Table 3

Effect of pH on Drug Loading

The pH of the media also affects the extent of drug loading. When zolpidem tartrate was loaded into resin in different pH environments, it was observed that optimum drug loading was achieved at pH 6.8 and further decreased at pH higher than this. The data is reported in Table 4.

Characterization of Drug Resin Complex

Physical characterization of resinate

The Micromeratic properties of resinate powder were determined using a bulk density apparatus and flow properties **(**angle of repose, compressibility index and hausner ratio) were evaluated as per methods described in USP. The results were shown in Table 5. All the quality control parameters were found in range as per the specifications given in official references.

Molecular Properties of Drug-Resin Complexes

Thermal analysis: The thermogram of Zolpidem tartrate shows a sharp endothermic peak at 296.94°C corresponding to melting of pure drug and its crystalline nature. The thermogram of Tulsion 335 indicates its amorphous nature. The thermogram of Resinate indicates its amorphous nature and shows the absence of endothermic peak of melting of the drug (Figure 1). The formation of Resinate and entrapment of Zolpidem tartrate in the polymer matrix of Tulsion 335 was thus confirmed from the findings of these three studies.

X-ray diffractometry: The x-ray diffractograms of Zolpidem tartrate confirmed its crystalline nature, as evidenced from the number of sharp and intense peaks. The diffractograms of Tulsion 335 showed diffused peaks, indicating its amorphous nature while the diffraction pattern of resinate represents complete disappearance of crystalline peaks of drug. These findings suggested that the drug was completely entrapped in the resin polymer matrix (Figure 2).

Fourier-transform infrared spectrophotometry: Pure Zolpidem tartrate spectra showed sharp characteristic peaks. All the above characteristic peaks appear in the spectra of resinate at same wave number indicating no modification or interaction between the drug and carrier (Figure 3).

Determination of *In Vitro* Drug Release

Release of Zolpidem tartrate from resinate in three different pH media is shown in figure 4. Resinate showed the maximum release of drug in 0.1 N HCl (pH 1.2) due to cleavage of bond between the drug and resin. At pH 6.8 similar condition to saliva showed less release of drug confirms that the removal of bitter taste of drug. At pH 6.8 in time interval of one minute 0.05 mg drug was released which has not enough bitter taste sensation. The neutral medium (pH 7.4) showed very less drug release.

Taste Evaluation

The volunteers did not report any bitterness for drug resin complex throughout the study. From these outcomes of *in-vivo* evaluation, it was concluded that the taste masking of zolpidem tartrate by making an ion exchange complex with Tulsion 335 was complete and satisfactory.

Evalution of Zolpidem Tartrate Mouth Dissolving Tablets

The fabricated mouth dissolving tablets were tested for their physical parameters viz. diameter, thickness, hardness, weight variation, disintegration time and friability. The results are tabulated in table 7.

DISCUSSION

Factors and Process Affecting Zolpidem Tartrate Resinate Formation

In the present investigation, the tablets are prepared by conventional direct compression method where the drug resin ratio is 1:3 because maximum drug loading was achieved at D:R (1:3) in resinates. As D:R ratio increases from 1:1 to 1:3, increases drug loading was observed. This is because of the increase in amount of resin, higher is the resin; greater will be the number of exchangeable groups making more number of free cations available for adsorption pocess. Hence, more amount of drug will get adsorbed on resin. As we further increase D:R ratio decreases in resin .this may be because of saturation in amount of drug loading onto resin as shown in (Table 1) . The resin requires proper swelling time for maximum drug loading. It was concluded that a swelling time of 60 minutes was sufficient for maximum swelling of ion exchange resin. Swelling and hydration increases the rate and extent of ion exchange process. In unswollen resin matrix, the exchangeable groups are latent and coiled towards the backbone. Swelling increases the surface area and these groups get oriented towards outside (Table 2).

The effect of complexation time on drug loading it was found that with increase in time for stirring the solution, the drug loading gets increased and maximum drug loading was achieved at 4 h. This may be due to increases in contact time between drug and resin so that more number of molecules of drug can displace the cations from the resin and itself get adsorbed. As the stirring time was further increased at 5 h, loading was not considerably increased because once the maximum drug adsorption is achieved the desorption of the drug from resin takes place (Table 3).The pH of the media also affects the extent of drug loading. When zolpidem tartrate was loaded into resin in different pH environments, it was observed that optimum drug loading was achieved at pH 6.8 and further decreased at pH higher than this. The mobile or exchangeable cation in Tulsion 335 is the Hydrogen ion. In acidic environments (generally pH below 4) the resin exists as free acid in an essentially nonionic state and all drug was released in filtrate and at pH 7.4 the solution becomes basic and cationic ions gets saturated with basic solution so ions cannot be attached with basic solution (Table 4).

After compression of powder, the tablets were evaluated for their physical organoleptic (colour, odour, taste) and quality control parameters (thickness, hardness, Friability, disintegration time and wetting time). The prepared tablets were elegant and also free from any surface texture problems.

Tablets prepared have low disintegration time and sufficient strength to withstand its integrity during handling and storage .The formulation with crospovidone showed maximum release than the tablets with Sodium starch glycolate and Ac-Di-Sol. The experiment proved that the disintegration release was rate-limiting step from the tablet. So release of drug and release rate was higher from these tablets. From the observed data, it can be clear that less time in disintegration increases the release rate of zolpidem tartrate from Mouth Dissolving Tablet.

CONCLUSION

In the present investigation, a complex of Zolpidem tartrate was successfully formulated using Tulsion 335 resin, which was confirmed using FTIR, XRD and DSC. The volunteers rated the resinate as tasteless and agreeable complex. The methods designed for drug resinate complexation and tablet formulation is simple, rapid, cost effective and highly efficient. It was concluded that mouth dissolving tablet of resinate can be successfully prepared by super disintegrant addition and was found to be disintegrate less than 1 minute, which provide faster effect and better patient compliance.

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REFERENCES

1. Nanda AR, Kandarapu, Garg S. An Update on Taste Masking Technologies for Oral Pharmaceuticals. Indian J Pharm Sci 2002; 64: 7-10.
2. Lachman L, Liberman HA, Anig JL. Theory and practice of industrial pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1991.
3. Mantell CL. Ion exchangers. In: Adsorption. McGraw-Hill; 1951.
4. Betty W, Michael P, Dokuzovic V, Lam V. U.S. Patent (6001392) 1999.
5. Agarwal R, Mittal R, Singh A. Drug Dev. Ind. Pharm. 2000; 26:773–776.
6. Jenke DR. Pharm. Res. 1989; 6:96–99.
7. Irwin WJ, Belaid KA. Drug Dev. Ind. Pharm. 1987; 13:2017–2031.
8. Burke GM. Drug Dev. Ind. Pharm. 1986; 12:713–732.
9. Vercammen PJA. Int. J. Pharm. 1992; 85:45–50.
10. Hui H. Design and fabrication of oral controlled release drug-delivery systems. In: Robinson JR, Lee VHL, editors. Controlled drug delivery. Marcel Dekker; 1987. p. 412–414.
11. Patat A, Naef MM, Gessel VE, Forster A, Dubruc C, Rosenzweig P. Flumazenil antagonizes the central effects of zolpidem, an imidazopyridine hypnotic. Clin Pharmacol Ther 1994; 56 Suppl 4:430–6.
12. Quaglio G, Lugoboni F, Fornasiero A, Lechi A, Gerra G, Mezzelani P. Dependence on zolpidem: two case reports of detoxification with flumazenil infusion. Int Clin Psychopharmacol 2005; 20 Suppl 5:285-7.
13. Venkatesh DP, Rao CGG. Formulation of Taste Masked Oro-Dispersible Tablets of Ambroxol Hydrochloride. Asian J Pharmaceutics. 2008; 261-264.

Table 1: Effect of concentration of resin on drug loading

D:R	Drug Percentage
1:1	43.42
1:2	67.36
1:3	86.98
1:4	88.87

Table 2: Effect of stirring speed and time on drug loading

Stirring Time (min)	50 rpm	100 rpm
	% Drug Loading	% Drug Loading
15	26.92	27.34
30	29.04	31.84
60	40.18	41.68

Table 3: Effect of complexation time on drug loading

Time (h)	% Drug Loading
1	43.16
2	57.89
3	74.62
4	89.21
5	90.92

Table 4: Effect of pH on Drug loading

pH	1 h	2 h	3 h	4 h
	% Drug loading	% Drug loading	% Drug loading	%Drug loading
1.2	16.81	21.76	29.33	37.23
6.8	49.05	65.14	78.10	84.86
7.4	33.47	49.13	62.81	69.12

Table 5: Physical evaluation of Resinate

Parameters	Resinate
Bulk Density (gm/cm^3)	0.611
Tapped Density (gm/cm^3)	0.702
Compressibilty Index (%)	12.962
Hausners Ratio	1.148
Angle of Repose	23.64

Table 6: Formulation of mouth dissolving tablets with Resinate

Ingredients	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
Drug resinates equivalent to 5 mg of zolpidem tartrate	35 mg	35 mg	35 mg	35 mg	35 mg	35 mg
Crospovidone	3 mg	4 mg	-	-	-	-
Ac-Di-Sol	-	-	3 mg	4 mg	-	-
SSG	-	-	-	-	3 mg	4 mg
MCC	26	26	26	26	26	26
Dextrose	15	15	15	15	15	15
Lactopress	15	15	15	15	15	15
Talc	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2

Table 7: Evaluation of mouth dissolving tablets

Ingredients	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
Thickness (mm)	2.313± 0.022	2.076± 0.121	2.329± 0.089	2.415± 0.025	2.361± 0.061	2.295± 0.066
Weight (mg)	99.133± 0.665	98.466± 0.737	99.4± 0.264	100.833± 1.450	97.233± 0.602	97.733± 0.321
Hardness (kg/cm^3)	2.713± 0.156	2.913± 0.200	3.043± 0.150	3.003± 0.090	2.800± 0.191	2.990± 0.101
Friability (%)	0.823± 0.051	0.64± 0.05	0.536± 0.030	0.626± 0.045	0.653± 0.081	0.856± 0.041
In Vitro Disintegration time (s)	51.66± 2.51	20.66± 2.08	62.66± 2.516	38.00± 3.00	66.33± 3.05	41.66± 1.52
Wetting time (s)	47.33± 6.02	18.66± 2.51	57.66± 3.51	32.33± 3.51	55.66± 6.11	38.33± 2.08
In Vitro Dispersion. Time (s)	57.33± 1.52	26.33± 2.08	63.63± 2.08	31.33± 2.51	68.66± 2.08	46.00± 2.64

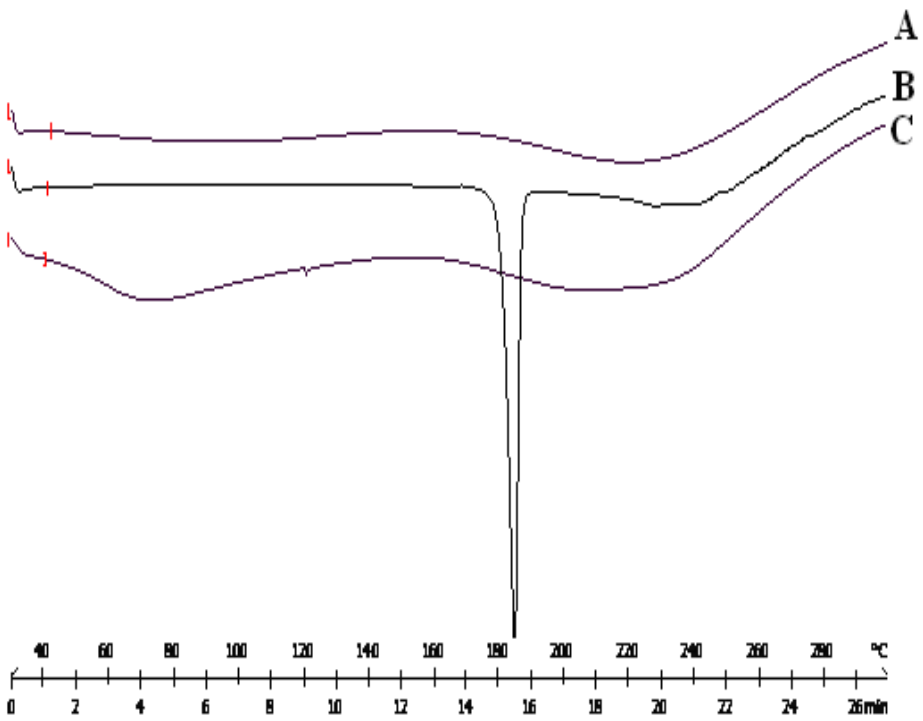

Figure 1: DSC Thermograms of Tulsion335 (A), Zolpidem Tartrate (B) and Resinate(C)

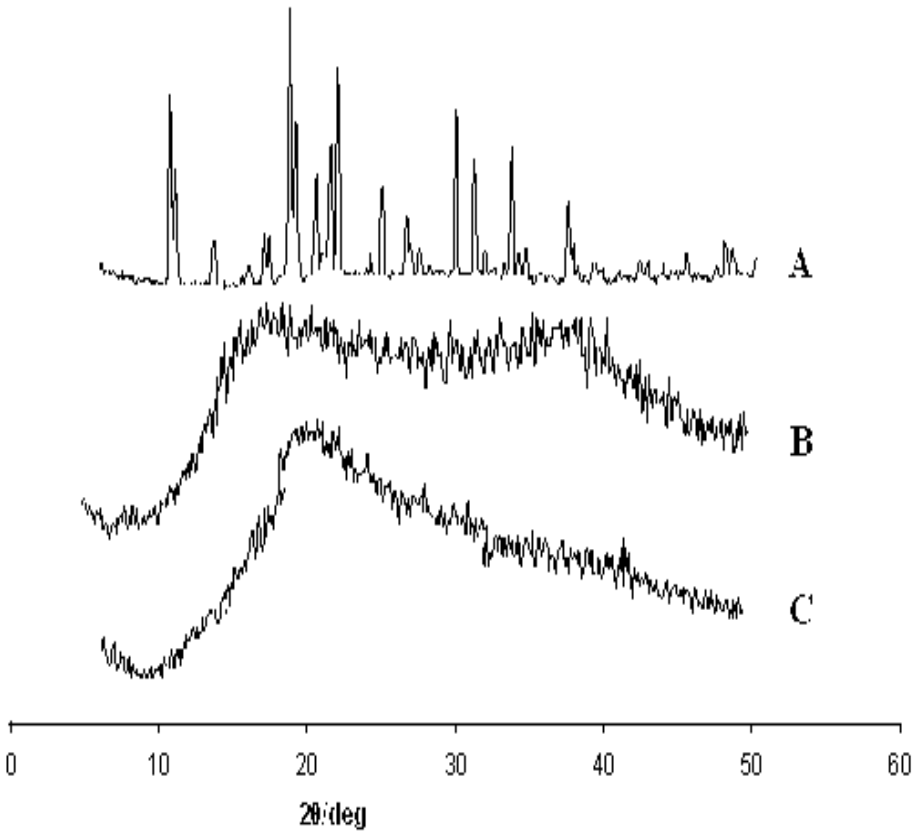

Figure 2: X-ray Diffraction Patterns of Zolpidem tartrate (A), Tulsion 335 (B) and Resinate(C)

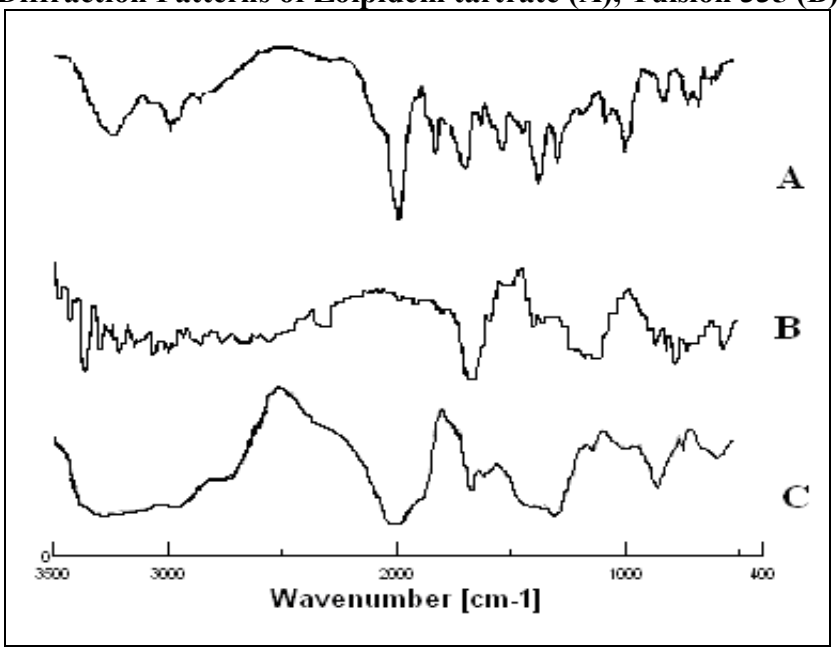

Figure 3: FT-IR Spectra of Zolpidem tartrate (A), Tulsion 335 (B), and Resinate (C)

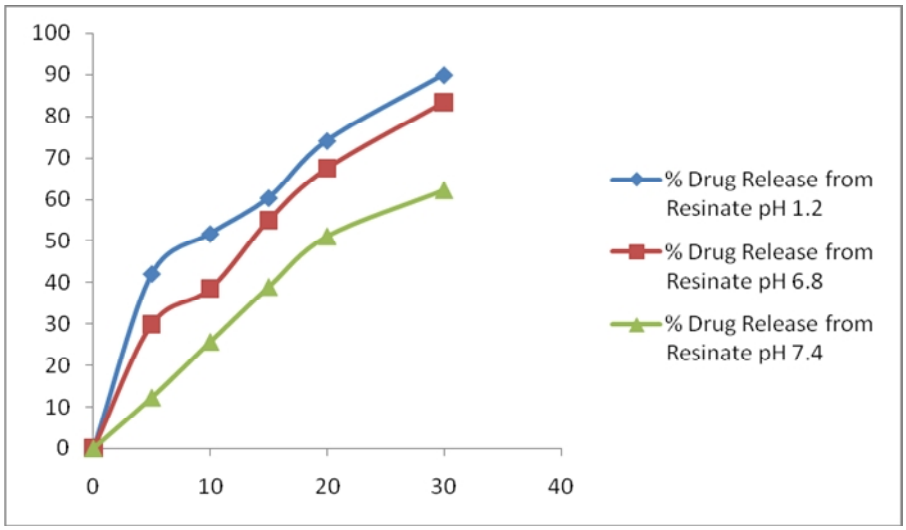

Figure 4: *In Vitro* Dissolution of Drug Release in pH (a) 1.2▲ (b) 7.4 ● (c) 6.8■

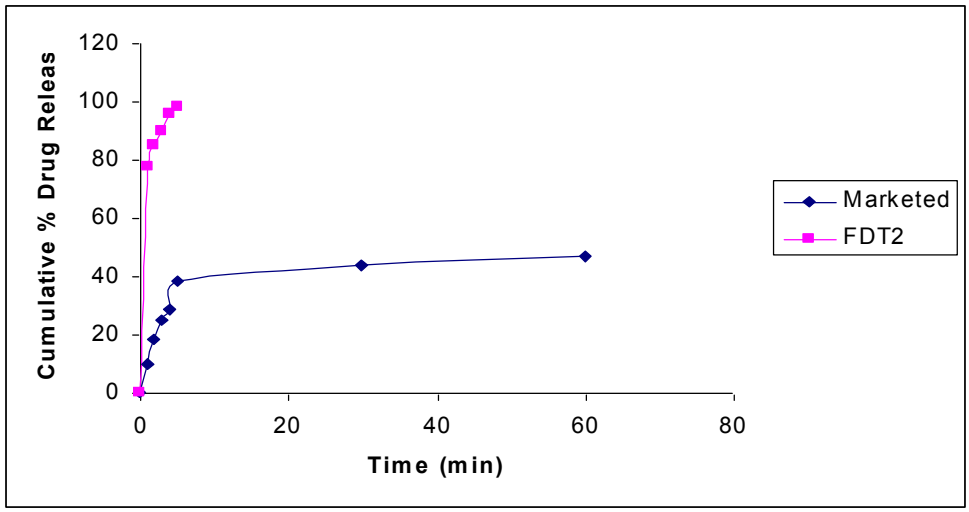

Figure 5: I*n Vitro* release Curve of FDT2 and Zolpidem Tartrate Marketed Tablets

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