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Studies on Multimedia Dissolution Profile of Zolpidem Tartrate Sustained Release Matrix Tablets

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ABSTRACT

The present study was focused on the effect of multimedia dissolution profile on the drug release of Zolpidem tartrate sustained release matrix tablets.Zolpidem is a relatively new non-benzodiazepine sedative/hypnotic used for short-term treatment of insomnia.Zolpidem is a widely used hypnotic agent acting at the GABAA receptor benzodiazepine site and show anxiolytic, sedative, myorelaxant and anticonvulsant, hypnotics properties.Zolpidem tartrate extended release tablets are prescribed for the treatment of insomnia in adults and they are known more commonly as sleep medicine.Hydroxypropyl methylcellulose (HPMC) is cellulose ether which may be used as the basis for hydrophilic matrices for controlled release oral delivery.Multimedia dissolution studies is to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption. The study ensures the impact of pH changes on dissolution and release of drug substance for absorption.

Keywords: Zolpidemtartrate , HPMC

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INTRODUCTION

Sustained release drug delivery system is designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. Zolpidem, the active moiety of Zolpidem tartrate, is a hypnotic agent with a chemical structure unrelated to benzodiazepines, barbiturates, pyrrolopyrazines, pyrazolopyrimidines, or other drugs with known hypnotic properties [1-3].Zolpidem tartrate is chemically known as N, N-,6-Trimethyl-2-ptolyl-imidazo(1,2-a)pyridine-3-acetamideL-(+)-tartrate. In contrast to the benzodiazepines, which non-selectively bind to and activate all BZ receptor subtypes, Zolpidem *in vitro* binds the BZ1 receptor preferentially with a high affinity ratio of the alpha1/alpha5 subunits.This selective binding of Zolpidem on the BZ1 receptor is not absolute, but it may explain the relative absence of myorelaxant and anticonvulsant effects in animal studies as well as the preservation of deep sleep (stages 3 and 4) in human studies of Zolpidem at hypnotic doses. Many known polymer are available for sustained release preparation. Hydroxypropyl methylcellulose (HPMC) is cellulose ether which may be used as the basis for hydrophilic matrices for controlled release oral delivery [4- 6]. Multimedia dissolution is to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption [7-9].

MATERIALS AND METHODS

Zolpidemtartrate were obtained as a gift sample and tablets were prepared by direct compression using HPMCK_4M and HPMCK_{15}M polymer combinations. Other excipients used were Magnesium stearate, Talc, MCC and dibasic calcium phosphate. The drug content in each tablet was 12mg**.**

Physical Characterization

The tablets were subjected to their physical characterization. Hardness, friability and weight variation and found within the probable limits, Table [1].

Table [1]

FORMULATION		Weight Mean ± SD mg	Hardness Kg Mean± SD	Diameter (mm) Mean ± SD	Thickness (mm) mean	Friability (%)	Assay (%)
HPMC K4M mg	HPMC K15M mg						
15	10	120-1.465	5.5O- 0.14	6.80-0.015	2.80-0.015	0.50	95.83

Experimental

Three tablets of Zolpidem (120 mg each) were taken into three different pH of phosphate buffer (pH2.4, pH 6.8 and pH 7.5).The USP dissolution apparatus was set at rotation 50 rpm and temperature of the assembly was set at 37^0 C. The tablets were placed in above

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prepared three different media of different pH. Absorbance was determined at 275 nm by collecting sample at different time interval as follows 0.5,1,2,3,4,6,8 hrs. The percentage drug release were calculated at different time intervals at different pH . The graph was plotted between percent drug release and time for different dissolution media.

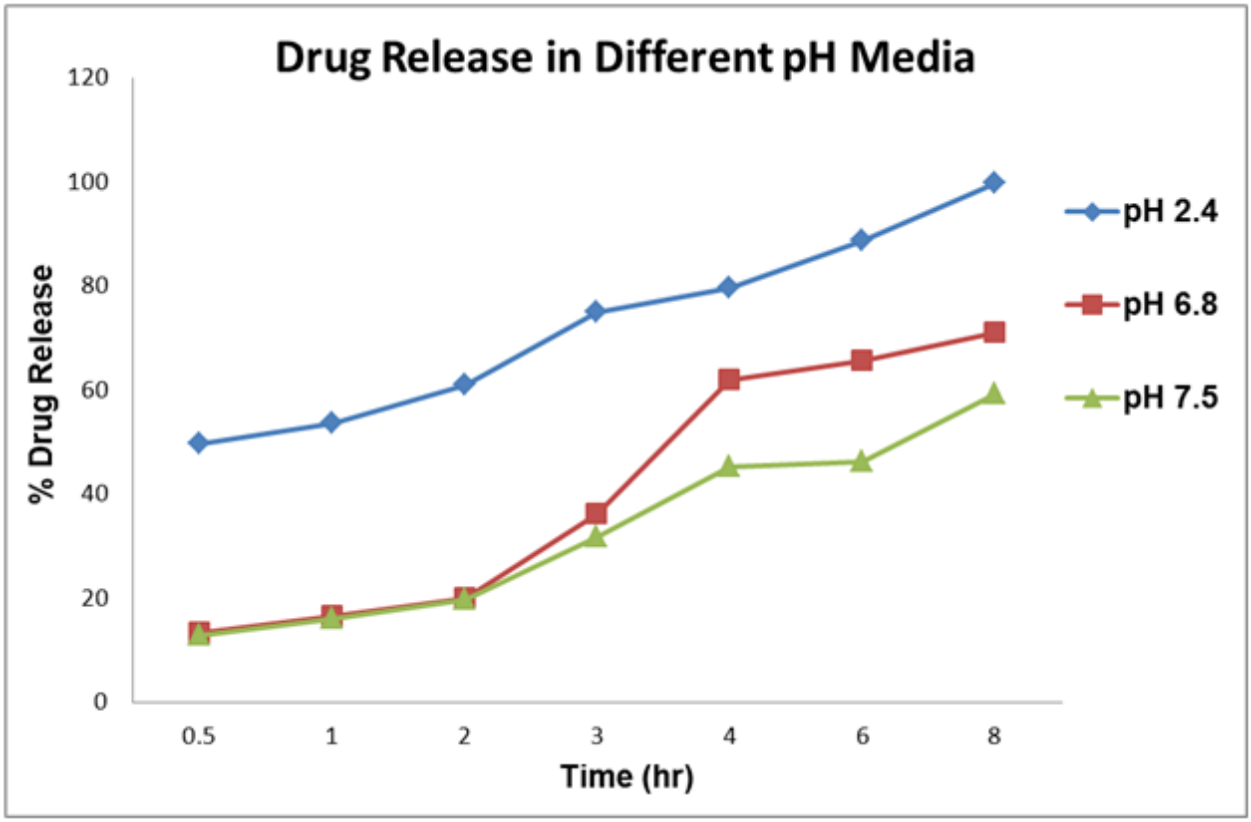
RESULTS AND DISCUSSION

Multimedia dissolution is to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption, [Table.2]. The graph shows thpercent drug release pattern at different time intervals for different dissolution medias at different pH [Fig.1].

Table [2]

Sr. No.	Time(hr)	Absorbance at different pH			% Drug Released in Different pH		
		2.5	6.8	7.5	2.5	6.8	7.5
1.	0.5	0.477	0.166	0.160	49.77	13.50	12.80
2.	1	0.511	0.192	0.189	53.74	16.53	16.18
3.	2	0.573	0.222	0.219	60.97	20.03	19.68
4.	3	0.692	0.361	0.322	74.85	36.24	31.69
5.	4	0.732	0.581	0.438	79.51	61.90	45.22
6.	6	0.811	0.612	0.447	88.73	65.52	46.27
7.	8	0.906	0.659	0.559	99.81	71.00	59.34

Fig.[1]



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CONCLUSION

The release profile of zolpidem from the matrices increased continuously with time, and the amount of drug release best seen in acidic media (pH=2.4). The cumulative amount of drug release is higher at pH 2.4 than that of pH 6.8 by 18 % and then that of pH 7.5 by 40 %. This increase in drug release at lower pH can be attributed to pH dependent solubility of ofzolpidem. As the pH decrease, the solubility of zolpidem increases which might increase drug release from matrices.

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