Global Journal of Medical Research: B
Pharma, Drug Discovery, Toxicology and Medicine
Volume 14 Issue 3 Version 1.0 Year 2014
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Comparative Study of Different Brands of Alprazolam

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Abstract- Benzodizapenes are the most widely used anxiolytic drug. They have largely replaced barbiturates and meprobamate in the treatment of Anxiety because they are safer and more effective. Alprazolam belongs to this class of drugs, it is used for the treatment of the anxiety symptoms of panic disorders.Present study deals with a brief overview of the comparative study of different brands of Alprazolam tablets according to Pharmacopeia (BP) & United States Pharmacopeia (USP) . for this reason.3 differen brands of Alprazolam 0.5 mg tablets have been evaluated using quality control test of thickness, hardness, weight variation and friability to assess that whether these 3 brands are pharmaceutically equivalent.

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GJMR-B Classification : *NLMC Code: QV 37, QV 38*

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Comparative Study of Different Brands of Alprazolam

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Abstract- Benzodizapenes are the most widely used anxiolytic drug. They have largely replaced barbiturates and meprobamate in the treatment of Anxiety because they are safer and more effective. Alprazolam belongs to this class of drugs, it is used for the treatment of the anxiety symptoms of panic disorders.Present study deals with a brief overview of the comparative study of different brands of Alprazolam tablets according to Pharmacopeia (BP) & United States Pharmacopeia (USP) . for this reason.3 differen brands of Alprazolam 0.5 mg tablets have been evaluated using quality control test of thickness, hardness, weight variation and friability to assess that whether these 3 brands are pharmaceutically equivalent.

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I. Introduction

Alprazolam is a triazolobenzodiazepine. It is used in anxiety states and panic disorders [1, 2]. Benzodiazepines are commonly used for deliberate self poisoning. It has been observed that in approximately one third of cases of deliberate self poisoning benzodizapenes are being used[3]. Alprazolam is a newer benzodiazepine and is used more commonly in overdose and no previous series of alprazolam poisonings were found. 14 case reports have been published including 5 reported deaths,2 in which alprazolam was ingested alone [4]. According to reports published by American Association of Poison Control Centers National Data Collection System indicated that alprazolam was involved in thirty four fatal deliberate self poisonings over ten years 1992–2001 compared with thirty fatal deliberate self poisonings involving diazepam [5]. This reveals significant alprazolam toxicity if prescribing practices in the United States (US) mirror Australian trends where diazepam is prescribed at five to ten times the rate of alprazolam. A British study showed the fatal toxicity index (deaths per million prescriptions) for diazepam was 4.0 compared with 5.9 for alprazolam. [6]. These data suggest that alprazolam is more toxic in overdose than other benzodiazepines.

In human liver this drug is metabolized by CYP3A enzymes to hydroxylated metabolites . 4-hydroxy alprazolam (4-OHALP) is the major and less active metabolite while α-Hydroxy alprazolam (α-OHALP) is the minor and active metabolite. There is an intrinsic difference in the biotransformation of alprazolam in liver and brain. As P450 enzymes present in brain is one-10th to one-15th of liver [7]

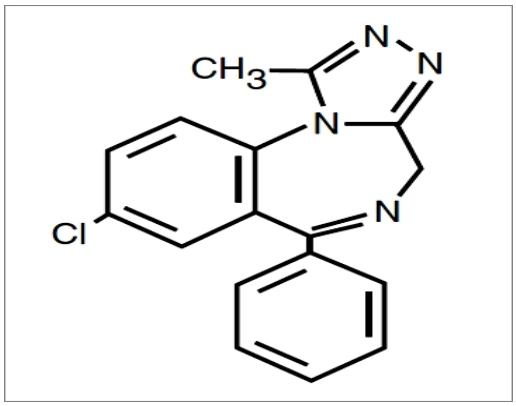

Figure 1 : Structure of alprazolam

II. Material and Methods

Alprazolam (0.5mg) tablets from the following thre different brands
Neuxam (stand pharmaceuticals)Batch P0315E
Alp (Hilton pharamceuticals) Batch 108891
Nervin (Werrick Pharmaceuticals) Batch 1971 Apparatus band equipments:

1. Analytical Balance
2. Rolex tablet hardness
3. Friability tester

The study used BP and other pharmacopeias to check the in vitro quality of alprazolam brands tablet using different analytical techniques and procedure described in the analytical techniques and procedures described in the pharmacopeias. For testing the physical parameters of alprazolam brands tablet Various instruments were used to measure content as well as qualities in general.

a) General Tests

Quality of alprazolam brands tablets were assessed in compliance with BP specifications. General tests include weight variation, tablets friability .

b) Weight Variation Test

Weight variation test of above mentioned tablets should be in accordance to the BP/USP requirements that not more than two tablets out of 20 tablets should cross ±7.5 % deviation.

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Table A : Limits for Uniformity of weight

Dosage form	Average weight	Percentage deviation
Uncoated and film coated tablets	80 mg or less More than 80 mg but less than 250 mg 250 mg or more	10 7.5 5

c) Hardness

The official range of hardness stated in BP/USP is not less than 4.00 Kg of pressure is required to break a tablet, so all of the samples were tested for hardness.

d) Friability

To evaluate how well the tablets stands up to coating, packing, shipping and other processing friability test were conducted. From each brand of legal and illegal products, 20 tablets were taken and de dusted before weighing, after weighing the tablet were placed in drum of friability tester of which each tablet rotated 100 times. Finally 20 tablets of each brand were de dusted and reweighed and their percentage losses of weight were calculated. According to BP & USP the total weight loss should not be more than one percent and no tablet should show any type of break or crack.

Thickness Test: Thickness of above mentioned tablets including average , standard deviation, upper and lower limits are in accordance with BP/USP

III. Results

Weight Variation Test: Wt. variation test of alprazolam tablets proved statistically that all the tablets were in accordance to the BP/USP requirements. (Table-1 2 & 3)

Thickness Test: Thickness of all tablets of alprazolam including average,(SD) standard deviation and upper/ lower limits are in accordance with BP/USP (Table-4&5)

Hardness Test: Hardness test of alprazolam was found to not be in conjunction with the stated guidelines as given in BP/USP (Table-6&7).

Friabilty Test: Friability of alprazolam tablets was less than 1%. Therefore it is compliance with the BP/USP standards. It's data is given in (Table-8).

IV. Discusion

Uniformity of weight is compendia standard while hardness and friability are non compendia standards to assess the quality of the tablet. Friability is now included in USP.

a) Weight Variation

The table 1-3 indicate that weight variation values of Neuxam , Alp , Nervin showed that among three brands Alp has the highest value of the mean as compared to other brands. The requirements are met with weight variation qaccording to USP that is ,weight of not more than two tablets out of all brands differs from the average weight by more than 7.5%

b) Friability

The table 3 and figure 5(%weight loss for Nexaum , Alp , Nervin) showed that the Nexaum has the highest % weight lost and Alp has the lowest % weight lost when compared to Nervan.

All the three brands have less than 1% of weight lost which showed that these brands met the USP requirement.

c) Hardness

The official range of hardness stated in BP/USP is not less than 4.00 Kg of pressure is required to break a tablet, so all of the samples were tested for hardness.

The table and figure showed that Nervin has the highest hardness value and Alp has showed lowest hardness value. It shows that Alp showed to meet the USP requirement while the other two brands are beyond the USP limit.

Table 1 : Weight Of 20 Tablets (Randomly Selected) of Different Brands

Tablets	Neuxam	Alp	Nervin
1	179	195	165
2	173	199	158
3	180	200	150
4	178	200	156
5	180	202	159
6	190	200	156
7	190	203	151
8	178	205	156
9	179	198	160
10	176	205	154
11	173	200	160
12	176	195	158
13	180	199	151
14	177	203	156
15	173	198	150
16	179	202	165
17	180	200	156
18	190	199	154
19	190	202	158
20	176	200	160

Table 2 : Statistical Weight Variations

Tablets	Average (Gm)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
Neuxam	0.17985	0.005687	0.196911	0.162789
Alp	0.20025	0.002712	0.2083	0.19211
Nervin	0.15665	0.004308	0.16957	0.1437

Table 3 : Weight Variation Test

Tablets	Result (Gm)	BP/USP Specification	Deviation from BP/USP Specification
Neuxam Alp Nervin	0.17985 0.20025 0.15665	Deviation should be ±7.5%	Within specified limit

Table 4 : Thickness Of 10 Tablets (Mm)

Tablets	Neuxam	Alp	Nervin
1	3.3	3.2	3.2
2	3.4	3.1	3.2
3	3.3	3.2	3.2
4	3.2	3.1	3.2
5	3.5	3.1	3.1
6	3.3	3.1	3.1
7	3.3	3.1	3.1
8	3.5	3.1	3.1
9	3.4	3.1	3.1
10	3.3	3.1	3.1

Table 5 : Statistical Thickness

Tablets	Average Thickness mm	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
Neuxam	3.35	0.09	3.64	3.05
Alp	3.12	0.04	3.246	2.99
Nervin	3.14	0.05	3.29	2.98

Table 6 : Hardness Of 10 Tablets From The Optimised Formulation

Tablets	Neuxam	Alp	Nervin
1	7.69	2.19	12.2
2	5.05	2.5	12.0
3	6.14	2.47	11.7
4	7.40	2.41	15.2
5	7.88	2.21	12.1
6	7.306	2.05	10.2
7	7.16	1.92	13.2
8	7.73	2.73	14.9
9	7.60	2.45	13.2
10	3.91	1.95	13.8

Table 7 : Statistical Hardness

Tablets	Average (Kg)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
Neuxam	6.7866	1.335725	10.79377	2.779426
Alp	2.288	0.265949	3.085847	1.490153
Nervin	12.85	1.524795	17.42439	8.275615

Table 8 : Friability Test

no. of tablets	Result (%)	BP/USP Specification	Deviation from BP/USP Specification
Neuxam	0.615	Not more than1%	In specified limit
Alp	0.099		
Nervin	0.128		

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