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Study of Quality Control Parameters of antidepressant drug in Active Pharmaceutical Ingredient and Finished Forms

*Ram Prakash Aharwal[a], Sandeep Kumar Shukla[a] and Archna Pandey[a]
(a)Department of Chemistry
Dr. Hari Singh Gour University, Sagar, (M.P), INDIA

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ABSTRACT: Alprazolam belongs to a group of medicines called benzodiazepines. These medicines are thought to work by their action on brain chemicals. Alprazolam has sedative effects and is used to anxiety and panic attacks.
The purpose of the current study is to provide a systematic analytical technique for the determination of Beer's Range, Sandell's sensitivity, Molar absorptivity, Regression equation, standard deviation, Relative standard deviation.
The result obtained in this research by various quality control parameters have shown that dosage form of alprazolam parameter i.e. degree of hardness, friability percentage and disintegration time of the tablets were made by using the corresponding instruments. Weight variations were measured by analytical balance. The results indicate that the propose quality control parameter are simple, sensitive, accurate and reproducible and can be used for the routine determination of alprazolam in bulk and Pharmaceutical formulations.
Key words: Alprazolam, hardness, friability, disintegration time, weight variations, optical characteristics, regression data.

I. AIMS AND BACKGROUND

In the last decade, an emerging interest has been growing towards brain drug targeting where issues have been widely discussed [1-8]. The increasing awareness of the lack of rational and common efforts different and complementary research areas has pointed out the need for a deeper understanding and a closer collaboration among diverse research expersts [9].

Benzodiazepines are the most often prescribed drugs [10] belonging to the most numerous group of continuously developed anxiolytic therapeutic substances. They are characterised by relatively low toxicity and weaker drug-dependence properties, so that their withdrawal syndrome is milder then that of the classical sleep- inducing and sedative drugs. [11]

Alprazolam is a triazolobenzodiazepine, that is, a benzodiazepine with a triazolo ring attached to its structure. The chemical name of alprazolam is 8 chloro-1-methyl-6-phenyl-4H-5 triazolo [4,3-a] [12-14] Alprazolam is a white crystalline powder .

This medication may cause dependence, especially if it has been used regularly for an extended period of time, or if it has been used in high doses withdrawal after long term treatment should be slowly over a period of weeks (or even month) to avoid serious withdrawal symptoms such as agitation, panic, attacks, rebound anxiety, muscle, cramps and seizures.
We report herein, the hardness, friability disintegration time and weight variations of drug. [15]

II. EXPERIMENTAL

All the chemicals used were purchased from Fluka and Sigma Aldrich Ltd. Company, alprazolam pure form was gifted by Ethicare laboratories, India and alprazolam tablets were all purchased from domestic Indian pharmaceuticals market. The apparatus is friability tester, Hardness Tester; Disintegration Apparatus were used for the measurement of friability, hardness and disintegration time, respectively. Analytical balance was used measuring the variation of the weights of the tablets. UV-Vis spectrophotometer is also used throughout the study.

Determination of λ_{max} of alprazolam pure form

The pure form of Alprazolam was accurately weighed 10 mg and dissolved in 100 mL of methanol. The stock solution was further diluted 1 mL (above solution) in 10 mL methanol made up to the volumetric flask. The absorption spectra were obtained with UV-VIS Spectrophotometer (Elico 164) a scan range of 200-400 nm and determine the maximum absorbance of drug i.e. λ_{max} 222 nm.

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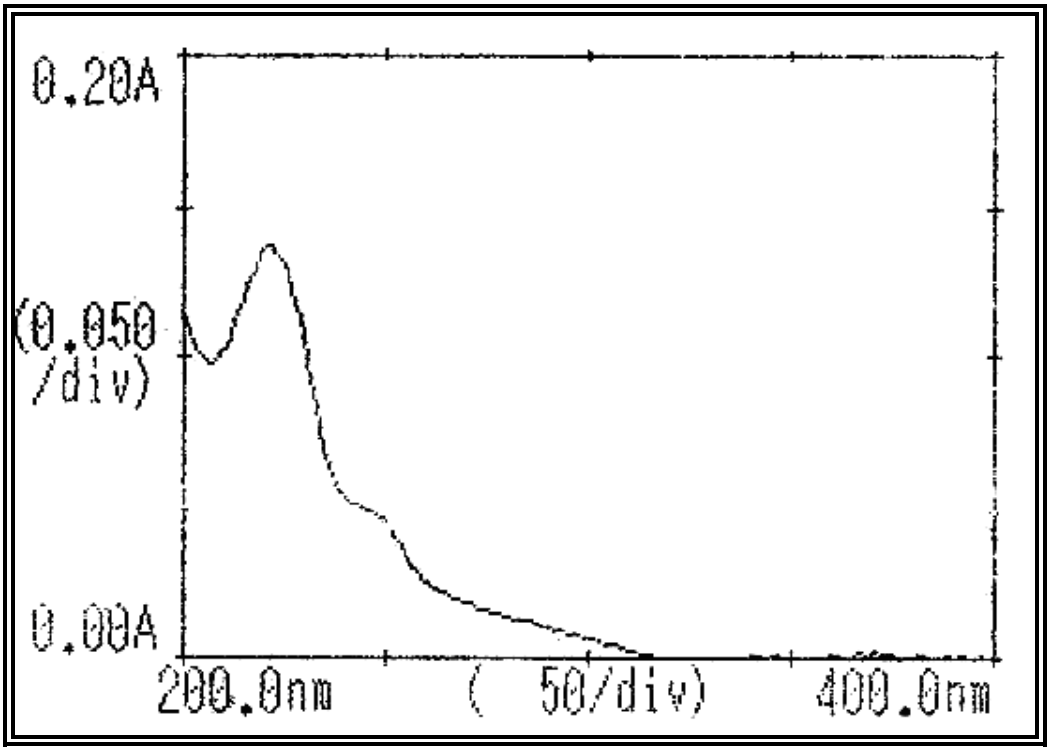
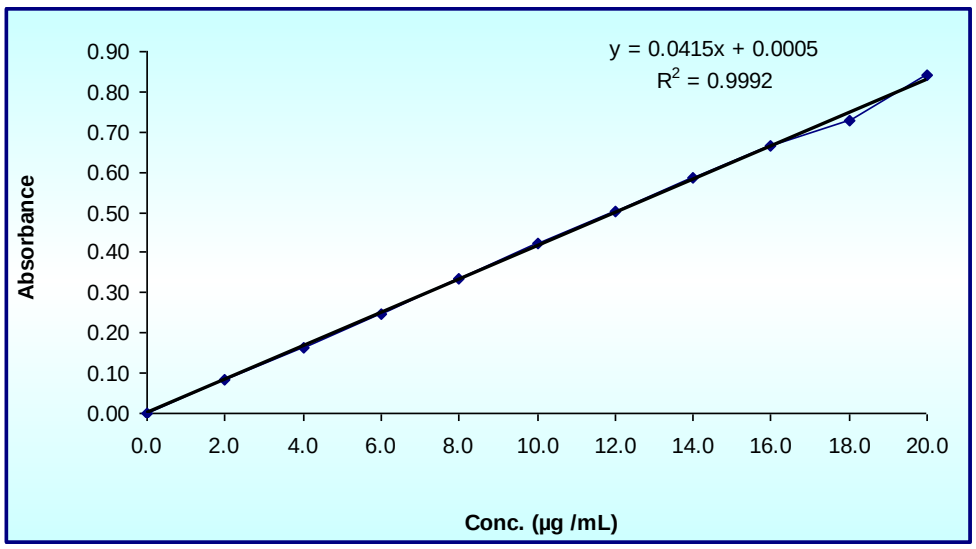


Plotting the standard calibration curve

An amount of 10 mg of pure alprazolam was dissolved in 100 mL of methanol in 100 mL volumetric flask. This stock solution was further diluted in the range 2-20 µg/mL and records the absorbance at λ_{max} 222 nm. A typical graph of the absorbance against concentration of alprazolam is shown in Fig.



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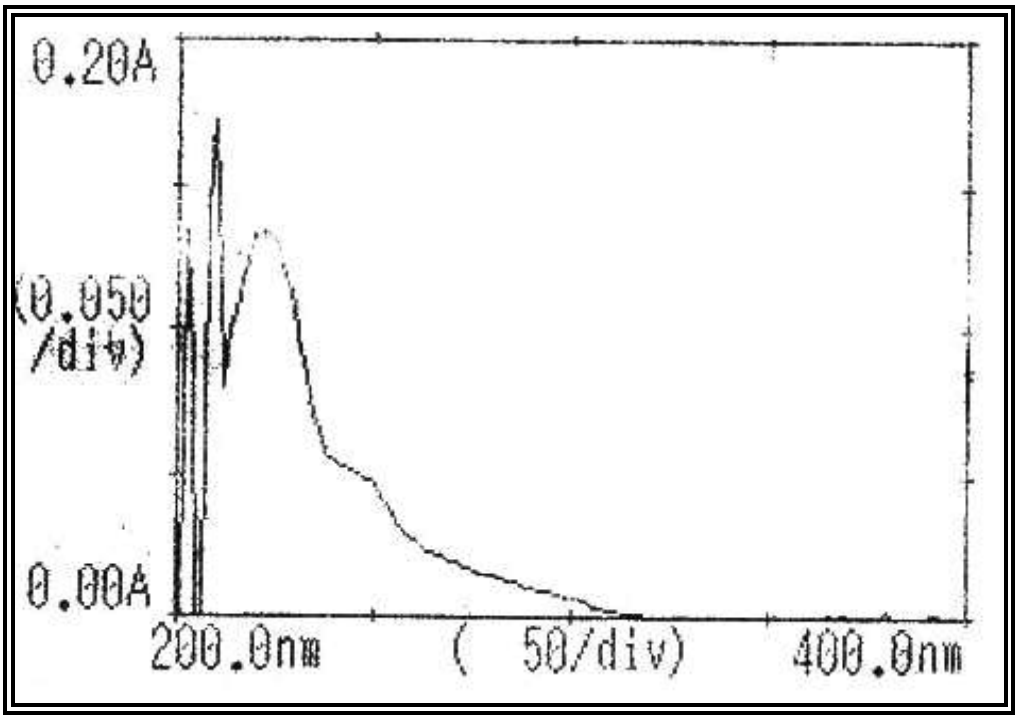
Determination of λ_{max} of alprazolam Finished Form

The finished form of Alprazolam was accurately weighed 10 mg and dissolved in 100 mL of methanol. The stock solution was further diluted 1 mL (above solution) in 10 mL methanol made up to the volumetric flask. The absorption spectra were obtained with UV-VIS Spectrophotometer (Elico 164) a scan range of 200-400 nm and determine the maximum absorbance of drug i.e. λ_{max} 222 nm.



Plotting the standard calibration curve

For plotting the standard curve prepare 100 ppm standard solution of finished form of alprazolam. Then diluted and prepared different ppm solution by using standard solution. The calibration curve was plotted. The results are given table 1.

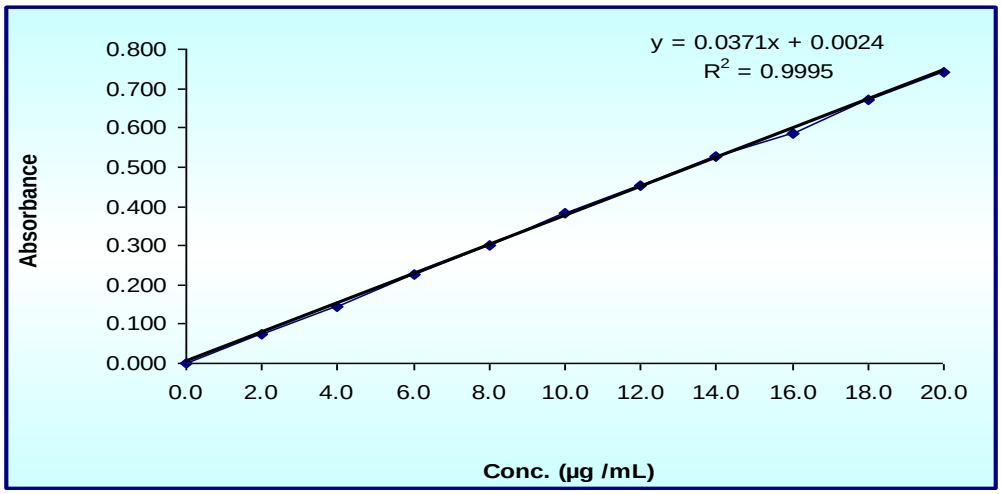


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Table-1 Optical and Regression Parameters of Alprazolam

Parameters	Results	
	API Form	Finished Form
Absorption Maxima λ_{max} (nm)	222	222
Beer's Lambert's limit (µg /mL)	2-20	2-20
Molar absorptivity (L $mol^{-1}cm^{-1}$)	1.29×10^3	1.14×10^3
Sandell's Sensitivity (µg cm^{-2})	0.238	0.269
Slope (m)	0.0415	0.0371
Intercept (c)	0.0005	0.0024
Correlation Coefficient (R^2)	0.9992	0.9995

Measuring the hardness of alprazolam tablets (Hardness test)

On the basis of the method reported in USP pharmacopaeia [16], 10 tablets of each of the three brand used in this research (Sample-A, Sample-B and Sample-C) were taken separately. The degree of hardness of each type was measured by the following procedure.

Each tablet was placed in the lower anvil of the instrument and the anvil was adjusted so that the tablet just touched the upper test anvil. The instrument was switched on, a suspended motor driven weight moved along a rail, which slowly and uniformly transmitted pressure to the tablet. A pointer moving along the scale provided the breaking strength value in kilogram/cm^2. As soon as the tablet started to break. The printer stopped. The results are given table. 2.

Table-2. Results obtained from the hardness test of alprazolam tablet (in kg/cm^2)

Sample	Minimum hardness	Maximum hardness	Average hardness	Standard Deviation	RSD
A	1.50	2.5	2.05	0.3	14.6
B	3.25	4.75	4.00	0.5	12.5
C	3.75	6.00	4.90	0.66	13.4

Friability test

On the basis of the methods reported in USP pharmocopoeia, 20 tablets from each of the three types of tablets used in this research were weighed separately. Each set of the tablets were placed simultaneously in the friability tester instrument. The instrument was set on 30 rpm for 2 minutes. After this, the tablets were removed and weighted again. Fraibility percentage of the tablets were calculated, the results are given in table.3.

Table-3 Results obtained from friability measurement

Sample	% Friability
A	0.38
B	0.15
C	0.00

Measuring the disintegration time of alprazolam tablets

The instrument is equipped with a basket containing 6 open ended tubes with the length of 7.5-8 cm and a diameter of 2.15 cm. A 10 mesh stainless steel sieve is placed under the tubes. The basket was placed in a 1liter beaker containing distilled water with temperature of 37±2ºC. The basket was moved upward and downward 25-30 times per minute to a height 5-6 cm in water. Each time, six tablets were taken randomly from each type of the tablets and to each open ended glass tube, one tablet was placed and covered with a special plastic sheet. Then, the instrument was turned on a disintegration time of each tablet was recorded. The minimum, maximum and average disintegration time of each tablet from each type of the brands were determined and recorded. The minimum disintegration time, was the time the first tablet started to disintegrate and maximum disintegration time was the time the last tablet started to disintegrate. The results are given in

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table-4. According to the general rute, the six coated tablets in distilled water must disintegrate in a period of upto 10 minutes.

Table-4 Results obtained from disintegration time measurement (min)

Sample	Minimum	Maximum	Average	Standard Deviation	RSD
A	1.91	2.58	0.23	0.24	10.7
B	0.25	0.35	0.29	0.04	13.8
C	0.21	0.28	0.25	0.02	8.0

Measurement of weight variations

20 tablets of each of the three types of the tablets were chosen randomly and weighed with a precise analytical balance (Contec-120). According to the authentic references the acceptable range should be with in 92.5-107.5% of the weight of the middle one. The results are given table-5.

Table-5 Results obtained from weight variation measurement (mg)

Sample	Minimum weight	Maximum weight	Average weight	Standard Deviation	RSD
A	129	132	130.1	0.83	0.63
B	129	131	130.15	0.58	0.44
C	129	131	130.1	0.49	0.37

III. RESULTS AND DISCUSSION

Regarding the efficacy of alprazolam and its rapid effect in patients, this is dependent largely upon the quality of the drug. It was decided to evaluate in vitro the following objectives between three types of alprazolam tablets produced domestically in India.

The optical characteristics and validation parameters [17] were given table. To evaluate the accuracy and reproducibility of the method known amounts of the pure drug was dissolved in methanol and diluted.

The value obtained for the determination of alprazolam in several pharmaceutical formulations and bulk drug, then proposed and reference methods were compared. The results indicate that the proposed methods are simple, sensitive, accurate and reproducible and can be used for the routine determination of quality control parameter of alprazolam in bulk and pharmaceutical formulations.

Determination of the degree of hardness, friability percentage and disintegration time of the tablets were made by using the corresponding instruments. Weights variations were measured by analytical balances. The various results obtained in this research have shown that:

1. Alprazolam tablets manufactured sample "c" had the highest where as those manufactured sample "A" had the lowest degree of hardness, respectively (Table.2).
2. Friability percentage of all three types of the tablets was with in the internationally well known pharmacopiea acceptable range (Table-3).
3. Disintegration times of all three of the tablets were within the expected range and sample "c" tablets and samples "A" tablet had the shortest and the longest disintegration time, respectively. (Table-4).
4. All of three types of the tablets used in this research were with in acceptable weight limits. (Table-5).

IV. CONCLUSION

In conclusion the results obtained in the research by various analytical quality control and physicochemical tests have shown that alprazolam tablets manufactured by sample "A" and sample "B" have the standard limits acceptable by the internationally well known pharmacopoeia such as USP and can satisfy the needs of patients quite well and are quite comparable with sample "C".

REFERENCES

[1]. Pardridge W.M., (2002), Drug Discov. Today, 7, 5-7.
[2]. Lawrence R.N., (2002) Drug Discov Today, 7, 223-226.
[3]. Lawrence R.N., (2002) Drug Discov Today, 7, 645-648.
[4]. Abbott N.J., (2004) Neurochem. Int., 45, 545-552.

[5]. Ghersi-Egea J.F., Sugiyama Y., (2004) Adv. Drug Deliv. Rev., 56, 1693-1694.
[6]. Pardridge W.M., (2001) Cambridge University Press, CAmbridge, U.K.
[7]. Ricci M., Blasi P., Giovagnoli S., Rossi C., (2006) Carr. Med. Chem., 13, 1757-1775.
[8]. Su Y., Sinko P.J., (2006) Drug Delivery, 3, 419-435.
[9]. Pardridge W.M., (2003) Mol. Interv., 3, 90-105.
[10]. Pakulska W., (2000) Farm.pol., 56, 250.
[11] Kostowski W., Kubikowski S., farmakologia, (1996), PZWL, Warszawa.
[12]. Florey K., (1980) Analytical profiles of Drug Substances, 9, 487.
[13] Singh S., Sathali A. A. H., Jayaswal S.B., (2002) Acta pharmaceutica Turcica, 44,105-118.
[14] Lachman L., Lieberman H.A., and Kanig J.L., "Theory and practice of Industrial Pharmacy", (1986), 3rd Ed. Philadelphia: Lea and Febiger, 297-304.
[15] Loftson T., Magnusdottir A., Musson M., Sigurjonsdoftir J. F., (2002) J. pharm .sci. 91, 2307.
[16]. O'neil M.J., "The Merk Index," (2001). 13th Ed, Woshington, Merck and Co. Inc, Whitehouse station, NY, USA, 310-311.
[17]. Srinubaby G., Sudharani B., and Seshagiri Ro J.V.L.N. (2006), e-journal of chemistry, 3, 9-12.