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RESEARCH ARTICLE

Invitro Studies of Different Brands of Cephalexin Monohydrate Capsules (500mg) Available In Local Market (Pakistan)

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Abstract

Drugs and health care structures are no more reliable for community because of substandard and poor quality medicines, which are dangerous for human health and life, so it is important to check the approved medicines to assess their efficacy and safety for the whole population. The present study is to investigate the invitro comparison of 5 different brands of cephalexin monohydrate capsules available in Pakistan.The invitro parameters include dissolution rate, weight uniformity, disintegration time, and HPLC assay of cephalexin.This study reveals that weight of all brand of capsules lies within the pharmacopeia limit, that is +-7.5%. dissolution process was carried out according to USP method and potencies of all brands were within the specified range, that is not less than 80% of the labeled amount is dissolved in 30 minutes (USP 2007), and all capsules disintegrates within 5 minutes that lies in the USP range, according to USP maximum time for capsule disintegration is 15 minutes. Overall purpose of the study is to provide safe interchangeable drug to the public.

INTRODUCTION

MATERIAL AND METHOD:

DRUG:

Cephalexin monohydrate

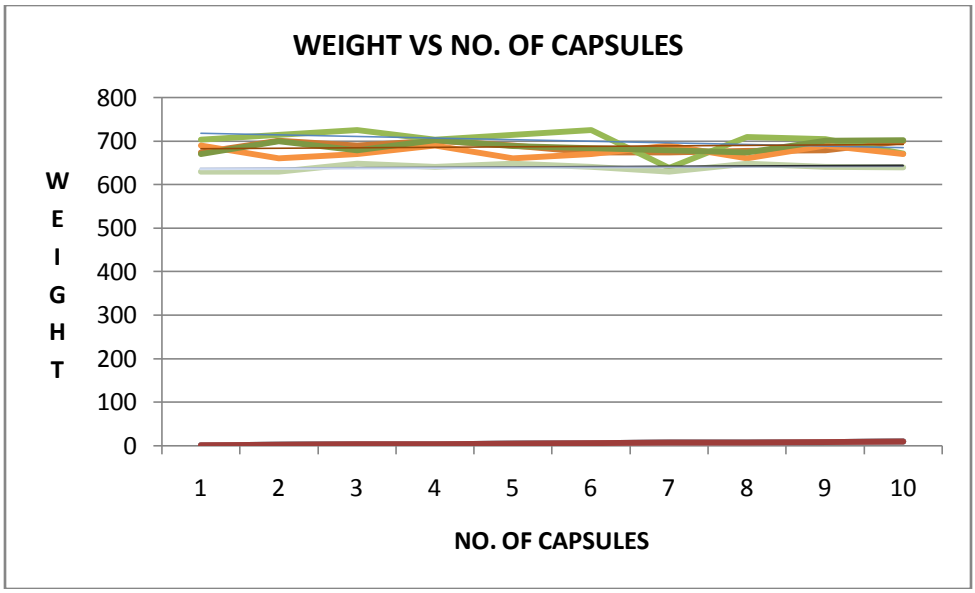
EQUIPMENTS:

Dissolution apparatus I, UV-Spectrophotometer (Gamma, England), Electrical balance (Schimadzu LC solution 1.23 Japan), Disintegrator.

WEIGHT VARIATION:

Capsule is a single unit dosage form containing specific amount of active ingredient. Weight of capsule is measured to check whether capsule contain specific amount of drug or not.

10 capsules from 5 different brands were weighed individually and their average weight has been calculated.



Brand	Capsule No.	Weight(mg)
C-1	1	673.9
	2	701.2
	3	690.1
	4	701.1
	5	690.2
	6	673.9
	7	673.9
	8	678.1
	9	679.4
	10	700.5
C-2	1	704.2
	2	714.5
	3	725.7
	4	704.3
	5	714.3
	6	725.6
	7	639
	8	710
	9	705
	10	672
C-3	1	689.8
	2	660.8
	3	670.6
	4	689.7
	5	660.9

	6	670.6
	7	689.2
	8	660.4
	9	689.8
	10	670.4
C-4	1	630.2
	2	630.3
	3	648.1
	4	641
	5	648
	6	641.2
	7	630.2
	8	648.4
	9	641.2
	10	640.4
C-5	1	670.2
	2	700.1
	3	679.2
	4	702.1
	5	689.1
	6	684.2
	7	678.3
	8	673.9
	9	700.5
	10	702.1

DISINTEGRATION:

Disintegration is a very important parameter and is required to convert capsule into powder particles so that surface area of drug increases which helps in GI absorption. Prepare 0.6% v/v solution of HCl (Add carefully 16.2ml of 37% HCl into 500ml of distilled water and then make the solution upto 1000ml with distilled water) and fill the vessel of disintegration test apparatus with this solution upto recommended height. Maintain the temperature between 35 ^{o}C and 39 ^{0}C. Place 1 capsule in each of the 6 tubes of the basket and run the equipment. Start stopwatch and note the time when all capsules are disintegrated [1-2].

Brand	Disintegration Time (min.)	Percentage Assay (%)
C-1	3	100.81
C-2	3.5	99.1
C-3	3.8	100.95
C-4	3.6	99.6
C-5	4	99.13

DISSOLUTION RATE:

Dissolution is the mechanism of transferring solid drug particles into the solvent. Dissolution is very important because results obtained from in vitro dissolution can be co-relate with in vivo availability. It also provides critical parameters and basic information to design more effective dosage form. It is most reliable and sensitive interpreter of in vivo availability [3]. Quality of the product in the pharmaceutical dosage form can be predicted by dissolution. Batch to batch quality equivalence can be ensured by dissolution. After the finalization of formulation dissolution serves as quality control procedure.

Dissolution medium used is 900ml water. Apparatus used is USP I which runs at a RPM of 100. Sample was taken after every 5 minutes [4].

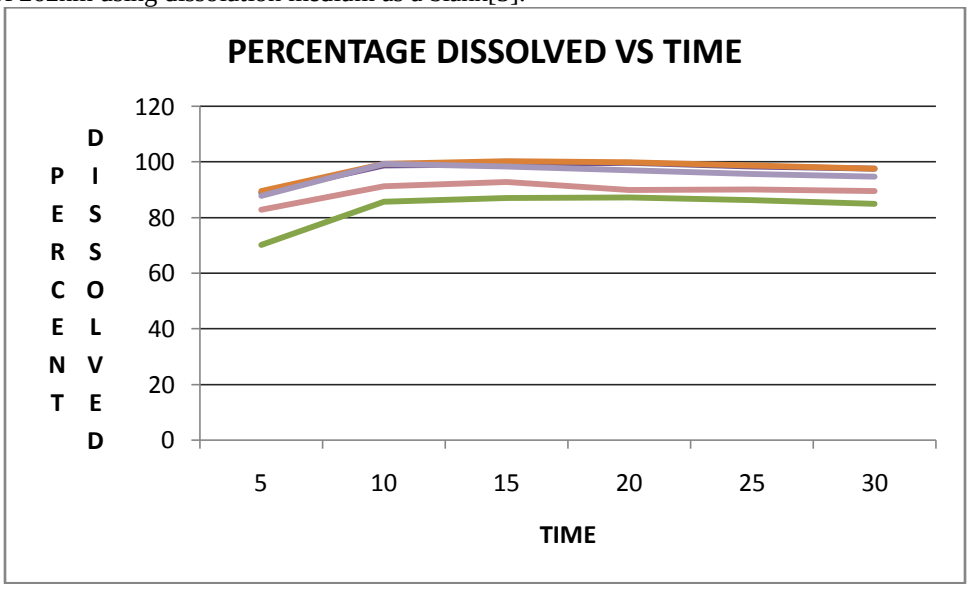
STANDARD PREPARATION:

Weigh accurately 0.020gm of Cephalexin standard in 100 ml of volumetric flask and dissolve in dissolution medium. Pipette 5ml of the above solution into 50ml volumetric flask and dilute the volume with dissolution medium and shake well.

SAMPLE PREPARATION:

Place 1 capsule each in 6 dissolution flask containing 900ml of dissolution medium previously adjusted to 37 ^{o}C ±0.5 ^{O}C and immediately operates the apparatus. After every 5 minutes withdraw the sample from a zone midway between the surface of medium and top of the rotating blade not less than 1 cm from vessel wall. Filter the sample [5].

Pipette 2ml of he filtered solution into 50ml volumetric flask and make up the volume with dissolution medium and mix well. Measure the absorbance of standard as well as sample preparation on a spectrophotometer at the wavelength of 262nm using dissolution medium as a blank[5].



Brands	Time (min.)	Percentage Dissolved.(%)
C-1	5	88.93
	10	98.73
	15	99.15
	20	99.722
	25	98.42
	30	97.6
C-2	5	89.62
	10	99.46
	15	100.35
	20	100.03
	25	98.77

	30	97.6
C-3	5	82.97
	10	91.27
	15	92.85
	20	90.06
	25	90.22
	30	89.59
C-4	5	87.86
	10	99.43
	15	98.48
	20	97.03
	25	95.76
	30	94.72
C-5	5	70.25
	10	85.827
	15	87.12
	20	87.34
	25	86.39
	30	84.97

ACTIVE INGREDIENTS ASSAY:

CHROMATOGRAPHIC SYSTEM:

High performance liquid chromatography method was used for the assay according to BP specification. A stainless steel analytical column of 150×4.6mm i.d packed with SS-ODS2. Pre column used is of 50×4.6mm.i.d stainless steel column packed with 80µm Porasil fitted between the pump and injector [6].

DETECTOR CONDITIONS:

254nm range of 0.5aufs.

PUMP CONDITION:

Flow rate 1.0ml/minute

INJECTION VOLUME:

20µL

MOBILE PHASE:

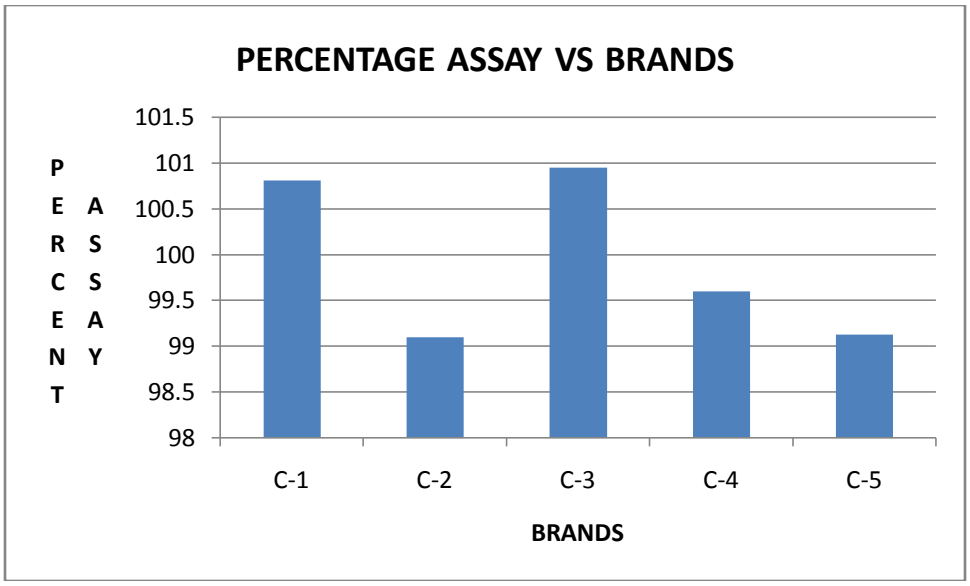
Dissolve 1gm Pentanesulfonic acid Sodium Salt (Monohydrate) and 15ml of Triethylamine in 850ml of distilled water; adjust the pH to 3.0 with orthophosphoric acid. Add 50m of Methanol and 100ml of Acetronitrile. Mix well and degas before use [7].

INTRERNAL STANDARD SOLUTION:

Dissolve 1gm of 1-Hydroxybenzotriazole in 1000ml of mobile phase, mix well.

SAMPLE PREPARATION:

Take 20 random capsules from composite sample and note individual weight content of each capsule and determine average content weight of 20 capsules. Accurately weigh about 500mg sample from composite sample of weighed content of 20 capsules in 500ml volumetric flask and record the weight, add water to dissolve and make up the volume with water up to 500ml mix well and filter[8-9]. Take 20ml of this dilution in 100ml volumetric flask, add 30ml internal standard and then water up to 100ml, mix well and filter through 0.45µm filter paper. Standard working solution was prepared similarly. The content of Cephalexin in capsule was calculated from peak areas of the chromatograms of the test and reference standard solution [10-12].



Brand	Percentage Assay (%)
C-1	100.81
C-2	99.1
C-3	100.95
C-4	99.6
C-5	99.13

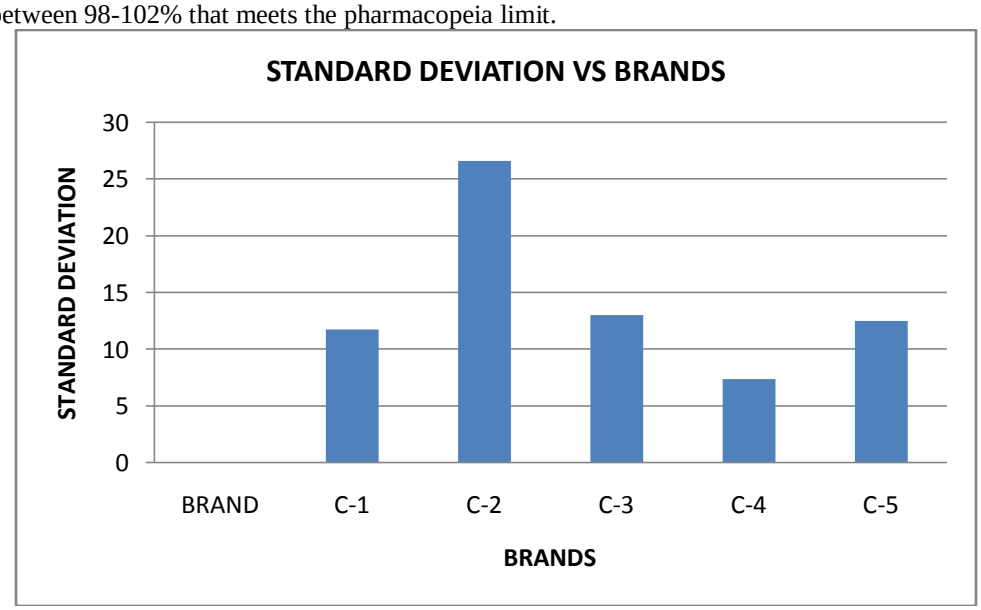
During the study, the brands available in the local market, of cephalexin capsule compiled with prescribed standards for disintegration time, dissolution time, weight variation and general characteristics. The hard gelatin capsules disintegration time was compiled with standard and all capsules disintegrate before 15 minutes as shown in table II. All products assay profile of cephalexin monohydrate is within the pharmacopeia limit, which is 92.5%-110% [13].
In all brands active ingredients are same but inactive ingredient may differ, due to which the dissolution profile varies but the dissolution profile shows that all brands can be interchangeable. There is no significant variation count between and within brands of cephalexin capsule [14].
The average weight of capsule is shown in table I and all the capsules meeting this pharmacopeia limit of weight.

S.No	Product Code	Manufactured by	Batch no./ Lot no	Mfg. Date	Exp. Date	Price
1	C-1	National Company.	196	Jun-13	Jun-15	155.80 Rs.
2	C-2	National Company.	4904	30-Apr-13	30-Apr-16	200 Rs.
3	C-3	National Company.	58	Oct-13	Oct-15	149.50 Rs.
4	C-4	Multi-National Company.	3E790	May-13	May-15	200 Rs.
5	C-5	National Company.	214	Aug-13	July-15	138.00 Rs.

Variation in the price of brands was seen while there is no significant difference in quality.
Table.1

DISCUSSION:

Cephalexin monohydrate was first sold by Eli lilly in 1972. The availability of many brands of Cephalexim 500mg capsules in Pakistan market today place health care providers in a difficult situation of choice of a suitable brand or alternate use possibility. Disintegration and dissolution are the main parameters for oral absorption of dosage form. Literature evaluation indicates that in developing countries substandard drugs are manufactured (Shakoor et al. 1997; Arya, 1997). Post marketing surveillance include complete procedures undertaken to obtain more data and information about a product after it had been granted marketing authorization and made available for public use, this data used for product improvement, development standard and regulations. Regulatory agencies rely on limited information get from clinical trials and from scientific literature as guide to grant marketing authorization of medicine for public use. Post marketing surveillance of approved dosage form is to assess the quality, effectiveness, and safe use of medicine to large population. In general drug substance factors such as solubility and permeability and physiological factors such as GI motility, GI pH, GI transit time, and GI fluid volume are same for same generic and reference product. While dosage form factors i.e. release rate and manufacturing factors are different for generic and reference products, so dissolution is the best method to detect these differences. Content assays shows safety and efficacy of a drug in a dosage form. The amount of Cephalexin in different brands, purchased from the market, was found between 98-102% that meets the pharmacopeia limit.



Brands	Standard Deviation
C-1	11.778
C-2	26.615
C-3	13.033
C-4	7.38
C-5	12.486

CONCLUSION:

In conclusion our result indicates that all brands of Cephalexin monohydrate capsules included in this study have good overall quality, and high dissolution rate which means good bioavailability. Its psychology of the human that generic medicine means poor quality but this study will help to change the view of people towards generic medicines.

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