CCET JOURNAL OF SCIENCE AND ENGINEERING EDUCATION

ISSN(Print) :2582-0680 ; ISSN(Online) :2455-5061 *Vol. – 6, Page-23-27 Year-2022*

STUDY OF PERCENTAGE PURITY, QUALITY OF THE DRUG IN DIFFERENT BRANDS OF CEPHALSPORINS

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Abstract

Drugs are the substance used in the prevention, diagnosis, treatment or cure of disease or as a component of medication. This is the era of competition and there are various pharma companies in the field. Some are really serving the mankind by genuine drugs but some pharma companies do not have such motive, they have only one motive "Money". Today various types of drugs are used for treatment of various diseases. They are Antibiotics, Antibacterial, Antifungal, Anti-inflammatory, Cardio-vascular drugs, Antiviral drugs etc. Today many people suffer from disease like fever, pneumonia, respiratory infection, skin infection etc. So, we have done the physiochemical study of different brands of Antibiotics (Cephalexin) comes under the category of antibiotic, Cephalosporin. It is 1st generation Cephalosporin. The main motive of this PAPER is to check the quality of different brand of API Cephalexin, sold in market and consuming by human beings. For this we have taken 4 brands of different tablet, capsule of same API. By this study we have another profit of gaining knowledge of drugs and about the work line of quality control test.

Index Terms: *Cephalexin, Antibiotic, bacteria, microorganisms.*

1. INTRODUCTION

Physico chemical study and the comparative study of various brands of API cephalexin were carried out. We will first describe about antibiotic and cephalosporin and then about cephalexin because cephalexin is a first-generation cephalosporin antibiotic.

Advances in medicinal chemistry, most antibiotics are now semi synthetic, modified chemically from original compounds found in nature, as is the case with beta-lactams (which include the penicillins, produced by fungi in the genus Penicillium, the cephalosporin's, and the carbapenems). Some antibiotics are still produced and isolated from living organisms, such as the aminoglycosides, and others have been created through purely synthetic means: the sulphonamides, the quinolones, and the oxazolidinones. In addition to this origin-based classification into natural, semisynthetic, and synthetic, antibiotics may be divided into two broad groups according to their effect on microorganisms: Those that kill bacteria are bactericidal agents, whereas those that only impair bacterial growth are known as bacteriostatic agents.[1]

Synthetic antibiotic chemotherapy as a science and the story of antibiotic development began in Germany with Paul German medical scientists in the late 1880s. Scientific endeavours to understand the science behind what cause these diseases, the development of synthetic antibiotic chemotherapy, the isolation of the natural antibiotics marked milestones in antibiotic development. [2]

These drugs were later renamed antibiotics by Selman Waksma, an American microbiologist in 1942.[3] Bacterial antagonism penicillium species were first described in England by John Zyndall in 1875. The significance to antibiotic discovery was not relizes until the work of Ehrlich on synthetic antibiotic chemotherapy, which marked the birth of the antibiotic revolution. Ehrlich noted that certain dyes would bind to and color human, animal, or bacterial cells, while others did not. He then extended the idea that it might be possible to make certain dyes or chemicals that would act as a magic bullet or selective drug that would bind to and kill bacteria while not harming the human host. After experimentation, screening hundreds of dyes against various organism's, discovered medicinally useful drug, which is the man-made antibiotic, Salvarsan.[4]

Because of their discovery of penicillin Ernst Chain, Howard Florey and Alexander Fleming shared the 1945 Nobel Prize in Medicine. Florey credited Dubos with pioneering the approach of deliberately, systematically searching for antibacterial compounds. Such a methodology had led to the discovery of gramicidin, which revived Florey's research in penicillin.[5]

Antibiotics are commonly classified based on their mechanism of action, chemical structure, or spectrum of activity. Most antibiotics target bacterial functions or growth processes.[6] Antibiotics that target the bacterial

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cell wall (penicillins, cephalosporin's), or cell membrane (polymixins), or interfere with essential bacterial enzymes (quinolones, sulphonamides) are usually bactericidal in nature. Those that target protein synthesis, such as the aminoglycosides, macrolides, and tetracycline's, are usually bacteriostatic.[6] Further categorization is based on their target specificity: "Narrow-spectrum" antibiotics target particular types of bacteria, such as Gram-negative or Gram-positive bacteria, whereas broad-spectrum antibiotics affect a wide range of bacteria. In the last few years, three new classes of antibiotics have been brought into clinical use. This follows a 40-year hiatus in discovering new classes of antibiotic compounds. These new antibiotics are of the following three classes: cyclic lipopeptides (daptomycin), glycocyclines (tigecycline), and oxazolidinones (linezolid). Tigecycline is a broad spectrum antibiotic, whereas the two others are used for Gram-positive infections. These developments show promise as a means to counteract the bacterial resistance to existing antibiotics.[6]

Cephalosporin - Cephalosporin compounds were first isolated from cultures of cephalosporium from a sewer in Sardinia in 1948 by Italian scientist Giuseppe Brown. He noticed that these cultures produced substances that were effective against Salmonella typhi, the cause of typhoid fever, which had beta- lactamase [7]. Guy Newton and Edward Abraham at the sir Willium Dunn School of Pathology at the University of Oxford isolated cephalosporin C[8].The cephalosporin nucleus, aminocephalosporanic acid was derived from cephalosporin C and proved to be analogous to the penicillin nucleus 6-aminopenicillanic acid, but it was not sufficiently potent for clinical use. Modification of the 7-ACA side-chains resulted in the development of useful antibiotic agents, and the first agent cephalothin (cefalotin) was launched by Eli Lilly in 1964 [7].

Mechanism of action:-

Cephalosporins are bactericidal and have the same mode of action as other beta-lactum antibiotics (such as penicillins) but are less susceptible to penicillinases. Cephalosporins disrupt the synthesis of the peptidoglycan layer of bacterial cell walls. The peptidoglycan layer is important for cell wall structural integrity. The final transpeptidation step in the synthesis of the peptidoglycan is facilitated by trans-peptidases known as penicillin-binding proteins (PBPs). PBPs bind to the D-Ala-D-Dla at the end of muropeptides (peptidoglycan precursors) to crosslink the peptidoglycan. Beta-lactum antibiotics mimic this site and competitively inhibit PBP crosslinking of peptidoglycan.[9].

Adverse effects

Common adverse drug reaction (ADRs) associated with the cephalosporin's therapy include: diarrhoea, nausea, rash, electrolyte disturbances, and /or pain and inflammation at injection site. Infrequent ADRs (0.1 -1% of patients) including: vomiting, headache, dizziness oral and vaginal candidiasis, pseudomembranous colitis, super infection eosinophilia, and /or fever.

MATERIAL AND METHOD

Sample and sampling - A portion of the universe drawn in the random fashion, but in such a way that it represent the chemical composition of the bulk material is called sample. The series of step, which ensure in procuring a sample material from the bulk material is known as the technique Or the sampling procedure. Very often, in the analytical process sampling turns out to be the most complex step. Precision and reliability of the method used to procure the sample it is therefore, essential to develop precise and reliable sampling techniques

Theory of sampling-

The theory of sampling is depend upon the law of statistical regularity. According to this law a moderately large no. of samples, elected at random from the universe and mixed homogenously to give average sample and is expected to represent the composition of universe with a high probability **Sampling**- Preservation of pharmaceutical drugs need sound knowledge of there physical and chemical properties. A good quality of the drug can be maintained if they are preserved properly we have collected 3 different samples of tablets containing cephalexin used as antibiotic.

DIFFERENT BRANDS OF CEPHALEXIN TAKEN FOR COMPARATIVE STUDY

TABLE-1

S.No.	Name of product	Make	Type
1	Nufex tablet	RPG Life Sciences	250 mg
2	Ceff tablet	Lupin	250 mg
3	Alexin capsule	Alembic limited	250 mg
4	Staphydex	Sandoz Pvt. Ltd	250 mg

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1.DESCRIPTION TEST

PROCEDURE: Take about 1.0gm of sample, blend in clean dry petri dish, observe virtually against black background.
OBSERVATION: white or almost white, crystalline powder of brightness 70-75% with characteristic odour.

TABLE -2

S.No	Sample name	Description	Result
1	Nufex Tablet	white or almost white, odour like beef extract.	Passed
2	Ceff tablet	white or almost white, odour like beef extract.	Passed
3	Alexin capsules	white or almost white, odour like beef extract.	Passed
4	Staphydex capsules	white or almost white, odour like beef extract.	Passed

2-SOLUBILITY TEST

THEORY: It is a test carried out for knowledge of purity. The test is carried out at the temperature 20-30°Corspecified in the individual monograph. GENERAL DATA FOR SOLUBILITY TEST is shown in Table 3

TABLE 3

S.NO	Terminology	Approx. Vol. of solvent in ml/gm of solute
1	Very soluble	Less than 1 ml
2	Freely soluble	From 1-10 ml
3	Soluble	From 10-30 ml
4	Sparingly soluble	From 30-100 ml
5	Slightly soluble	From 100-1000 ml
6	Very slightly soluble	From 1000-10000 ml
7	Insoluble/partially insoluble	More than 100000 ml

REFERENCE STANDARD: Slightly soluble in water; Partially insoluble in ethanol (95%), in chloroform and in ether.[10] as shown in Table 4

TABLE -4

S.NO.	Name of Sample	Observation	Result
1	Nufex Tablet	Slightly soluble in water; Partially soluble in ethanol (95%) Chloroform	Passed
2	Ceff tablet	Slightly soluble in water; Partially soluble in ethanol (95%) Chloroform	Passed
3	Alexin capsules	Slightly soluble in water; Partially soluble in ethanol (95%) Chloroform	Passed
4	Staphydex capsules	Slightly soluble in water; Partially soluble in ethanol (95%) Chloroform	Passed

3-IDENTIFICATION TEST: To identify the described API Cephalexin in different brands of drug.
PROCEDURE: FOR CAPSULE:
Shake quantity of the contents of the capsules equivalent to 0.5g of anhydrous cephalexin with 1 ml of water and 1.4 ml of 1M hydrochloric acid, filter and wash the filter with 1 ml of water. Add filtrate a saturated solution of sodium acetate until precipitation occurs. Add 5 ml of methanol filter and wash the precipitate with two quantities, each of 1 ml, of methanol. The residue after drying at a pressure not exceeding 0.7 kp is stored for further analysis. Mix 20 mg of the dried residue obtained in the above test with0.25 ml of 1% w/v solution of glacial acetic acid and add 0.1 ml of a 1% w/v solution of copper sulphate and 0.1 ml of 2M sodium hydroxide. An olive green colour is produced.[24]

FOR TABLET:
Identification: Shake a quantity of the powdered tablet cores equivalent to 0.5 g of anhydrous cephalexin with 1 ml og water and 1.4 ml of 1M hydrochloric acid, add 0.1 g of decolorizing charcoal, shake, filter and wash the filter with 1 ml of water. Add slowly to the filtrate a saturated solution of sodium acetate until precipitation occurs. Add 5 ml of methanol filter and wash the precipitate with two quantities, each of 1 ml, of methanol. The residue, after drying at a pressure not exceeding 0.7 kPa, complies with

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the test described above. Mix 0.25 ml of a 1% w/v solution of glacial acetic acid and add 0.1 ml of a 1% w/v solution of copper sulphate and 0.1 ml of 2M sodium hydroxide. An olive green colour is produced.[10]

TABLE-5

S.NO	NAME OF SAMPLE	OBSERVATION	RESULT
1	Nufex Tablet	An Olive Green Colour Is Produced	Passed
2	Ceff tablet	An Olive Green Colour Is Produced	Passed
3	Alexin capsules	Slightly soluble in water; Partially soluble in ethanol (95%) Chloroform	Passed
4	Staphydex capsules	Slightly soluble in water; Partially soluble in ethanol (95%) Chloroform	Passed

4-pH TEST:

PROCEDURE: The pH of solution is determined by electronic pH meter. A 0.5% w/v solution of sample is prepared and tested on electronic pH meter. Between 4.0-5.5[10] as shown in Table -6

5. QUANTITATIVE ANALYSIS

Determination of Assay: To a quantity of the powdered, mixed contents of 20 capsules equivalent of 0.25 gm of anhydrous cephalexin add 100 ml of water and shake for 30 minutes. Add sufficient water to produce 250 ml and filter. Using the filtrate so obtained, transfer 10.0 ml to a stoppered flask, add 5 ml of 1M sodium hydroxide and allow to stand for 20 minutes. Add 20 ml of a freshly prepared buffer solution containing 5.44% w/v of sodium acetate and 2.40% w/v of glacial acetic acid. Add 5ml of 1M hydrochloric acid and 25.0 ml of 0.02 iodine. Close the flask with the wet stopper and allow to stand for 20 minutes, protected from light. Titrate the excess of iodine with 0.02M sodium thiosulphate using starch solution, added towards the end of the titration, as indicator. To a further 10.0ml of the initial solution add 20ml of the buffer solution and 25.0 ml of 0.02M iodine, allow to stand for 20 minutes, protected from light and titrate with 0.02M sodium thiosulphate using starch solution, added towards the end of the titration, as indicator. The difference between the two titrations represents the volume of 0.02M iodine equivalent to cephalexin present. Calculate the content of $C_{16}H_{17}N_3O_4S$ from the difference obtained by simultaneously carrying out the assay using cephalexin RS instead of the substance being examined and from the declared content of $C_{16}H_{17}N_3O_4S$ in Cephalexin RS. Same titration is carried out with reference value

RESULT AND DISCUSSION:

A comparative study reveals the following facts related to physico- chemical analysis of cephalexin antibiotics. It gives the idea about the purity of API cephalexin. The sample was tested on following parameters:-Description, solubility, identification, pH, % assay. They are as follows

- Description gives the general appearance and it also represent the odor which is white powder of brightness 70-75% and the characteristic odor like beef extract, as described in std.test of cephalexin in pharmacopeia.
- The solubility gives the idea of purity. The compound should be slightly soluble in water, partially insoluble in ethanol (95%) and chloroform at 20-30°C. After performing this test we found that all samples of API follows this test.
-Identification test describes the presence of API . An olive green color is produced confirms the presence of API.
-pH reveals the acidic or basic nature of API. The range of pH as described in standard is 4.0-5.5. We found pH in following range: Nufex - 4.7, Ceff - 5.2, Alexin- 4.1, Staphydex -4 .8
- % assay is determined by lodometric titration. The specified limit for capsules is 90-110% and for tablet is 90-120%.

TABLE-6

S.NO	NAME OF SAMPLE	RESULT
1	Nufex Tablet	pH 4.7 obtained(Passed)
2	Ceff tablet	pH 5.2 obtained (Passed)
3	Alexin capsules	pH 4.1 obtained(Passed)
4	Staphydex capsules	pH4.8 obtained (Passed)

TABLE-7

S.NO.	VOLUME OF POTASSIUM CHROMATE TAKEN (ml)	VOLUME OF HYPO RUN DOWN(BURETTE READING)
1	10.0	09.9
2	10.0	09.8
3	10.0	09.8

TABLE-8

S.NO.	BURETTE READIMG (ml)	DIFFERENCE OF THE TWO READING(ml)
1	49.3	49.3 -49.2=0.1
2	49.2	

TABLE-9

S.N	Sample manufacture	BURETTE READING (ml)	Difference
1	Nufex Tablet (RPG LIFE SCIENCE)	1) 35.7 2) 42.5	6.80
2	Ceff tablet (LUPIN)	1) 40.6 2) 45.7	5.1
3	Alexin capsules (ALEMBIC)	1) 42.2 2) 47.5	5.3
4	Staphydex capsules (SANDOZ)	1) 31.9 2) 37.6	5.7
5	CORFEX SUSPENSION (CORWIS)	1) 17.9 2) 47.5	29.6
6	PHEXIN SYRUP(GSK)	1) 34.2 2) 48.6	14.4

TABLE-10

S.NO	SAMPLE NAME	MANUFACTURED BY	%ASS AY
1	Nufex Tablet	RPG LIFE SCIENCE	106.448 %
2	Ceff tablet	LUPIN	96.045 %
3	Alexin capsules	LUPIN	93.71%
4	Staphydex capsules	SANDOZ	104.61 %

CONCLUSION

An antibiotic is a substance produced by a microorganism that is antagonistic to the growth of other microorganism in high dilution. As antibiotic is a drug of great interest and work in many pharmaceuticals, by doing project under this field it is helpful in enhancing our knowledge and an idea of performing various test. Now a day's vitiation is increasing day by day in every sector including pharma sector also. Hence it is essential to check the quality of drug by its chemical analysis. During chemical analysis of antibiotic cephalexin parameters of testing for 6 brands of same API are taken, i.e. Nufex &Ceff tablet, Alexin & Staphydex capsule, Cortex & Phexin syrup.

At last we concluded that, there is a mark deviation in following sample: % purity for corfex suspension is 122 % LOD limit for Nufex is 1.67%& Phexin 1.84. (std. Limit NMT 1.5%) Deviation in sulphated ash test is for Ceff 0.72%, Staphydex 0.48% & Phexin 1.54% Hence we can say that chemical purity is an important criteria in all pharmaceutical industries and it should be properly checked to provide safe curation to human life.

REFERENCES

[1]. Davey P.G. (2000). "Antimicrobial chemotherapy" In ledingham JGG, lDA. Concise oxford textbook of Medicine.
[2]. SA Waksman (1947). "What is an antibiotic or an antibiotic substance?. httpp://jstor.org/stable/3755196
[3]. Kingston W June (2008). "Irish contributions to the origins of antibiotics" Irish journal of medical science 177 (2):87-9 .
[4]. Foster W, Raoult A (December 1974). "Early descriptions of antibiosis"..
[5]. Calderon CB, Sabundayo BP (2007): antimicrobial classifications: Drugs for Bugs. "Antimicrobial Susceptibility Testing Protocols". CRC Press.
[6]. Van Epps HL (2006). “Rene Dubos: unearthing antibiotics ".J.Exp.Med.203 (2) :259.
[7]. Pegler S, Herley B (10 November 2007). "In patients allergic to penicillin, consider second and third generation cephalosporin for life threatening infections". BMJ 335 (7627) : 991.
[8]. Rossi S, editor 2006." Australian Medicines Handbook. " .
[9]. Klayman DL. (September 2008). Cephalosporin’s and other beta-lactams". British National Formulary (56 Ed.). London: BMJ Publishing Group Ltd and Royal Pharmaceutical society Publishing. pp. 295.
[10]. Indian Pharmacopeia 2004.
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