



In Process Validation and Quality Parameters of Amoxicillin Potassium Clavulanate Tablet

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ABSTRACT

Amoxicillin was first introduced orally in the UK in the early 1970s, but gradually established itself as a broad-spectrum antibacterial it treats Infections of various diseases. Amoxicillin has been shown to be more effective against gram-positive microorganisms than against gram negative microorganisms. It has shown excellent efficacy against penicillin and penicillin V. Also, other antibiotics such as Ampicillin, azithromycin, clarithromycin, cefuroxime, and doxycycline are used to treat a variety of infections/diseases. Amoxicillin in the last 10 years. It has been reported to be useful in the treatment of many indications and is used to treat infections of the middle ear (otitis media), tonsils. (tonsillitis and tonsillitis), throat, larynx (laryngitis), pharynx (pharyngitis), bronchi (bronchitis), lungs (pneumonia), urinary tract (UTI), for skin and treatment of gonorrhea. Recent studies have shown that it can be used prophylactically against bacterial endocarditis in prosthetic patients.

Keywords: Antibacterial, Amoxicillin, Infection, Indications, Penicillin

1. INTRODUCTION

Amoxicillin is a penicillin derived antibiotic used against bacteria. It is used to treat many different types of infections caused by bacteria, such as tonsillitis, bronchitis, pneumonia, gonorrhoea, and ear, nose, throat, skin or urinary infections. Amoxicillin was discovered by scientists at Beecham Research Laboratories in 1972. The narrow spectrum of antimicrobial activity of the penicillin, led to the search for derivatives of penicillin which could treat a wider range of infections. The first important step forward was the development of ampicillin. Ampicillin had a broader spectrum of activity than either of the original penicillin and allowed doctors to treat a

broader range of both Gram-positive and Gram-negative infections. Further developments led to amoxicillin, with improved duration of action. It differs structurally from ampicillin merely by having an additional hydroxyl group on the benzene ring. The main difference between ampicillin and amoxicillin is that amoxicillin is slightly more lipid soluble. As a result, amoxicillin may kill bacteria slightly quicker. Amoxicillin acts by inhibiting the synthesis of bacterial cell walls. It inhibits cross-linkage of a major component of the cell walls of both gram-positive and gram-negative bacteria – linear peptidoglycan polymer chains. Amoxicillin first became available in 1972 and, today, there are many brands and forms of amoxicillin available. Amoxicillin clavulanate is the main antibiotic used in emergency and primary care settings nationwide. It is a combination of two drugs: amoxicillin and clavulanic acid. Amoxicillin is a penicillin derivative and has similar actions against gram-positive and gram-negative bacteria. In addition, the addition of clavulanic acid broadens the spectrum to include beta-lactamase-producing strains and extends coverage to other bacterial species. This

service reviews the indications, contraindications, dosage and side effects of amoxicillin clavulanate and emphasizes the role of a team of professionals in the effective use of this medicine. Amoxicillin clavulanate is the main antibiotic used in emergency and primary care settings nationwide. It is a combination of two drugs: amoxicillin and clavulanic acid. Amoxicillin is a penicillin derivative and has similar actions against gram-positive and gram negative bacteria. In addition, the addition of clavulanic acid broadens the spectrum to include beta-lactamase-producing strains and extends coverage to other bacterial species. This service reviews the indications, contraindications, dosage and side effects of amoxicillin clavulanate and emphasizes the role of a team of professionals in the effective use of this medicine.

2. MATERIALS AND METHODS

2.1 .WEIGHT VARIATION TEST =

$$\% \text{weight variations} = \frac{\text{average weight} - \text{individual weight}}{\text{average weight}} \times 100$$

Weight variation test is run by weighing 20 tablet individually calculating the original weight and comparing the individual Wight to the average weight.the value of weight variation test is expressed in percentage.

2.2 THICKNESS OF TABLET: The tablet thickness is determine by the diameter of tablet. Vernier caliper are used for checking tablet thickness. Thickness should be controlled within 5% variation of standard value. Thickness must be controlled for consumer acceptance for the product and to facilitate packaging.

2.3 HARDNESS OF TABLET: To conduct the hardness test randomly select and crushing strength of the tablet measure. The average hardness of the tablet calculated and the standard deviation determined. Hardness is measured by a instrument which is called as Monsanto test.

2.4 .DT: The tablet of Amoxicillin randomly selected and placed in the DT apparatus which is filled by 900ml of distilled water maintain at $37\pm 10^{\circ}\text{C}$. The time taken to disintegrate the tablet and pass through the mesh recorded and the mean of time taken calculated. It consists of a water bath which is filled upto mark mentioned a basket rack holding six plastic tubes open at top and the bottom is covered with a 10 mesh screen.

Procedure:

The basket rack assembly is suspended in liquid medium in 1000ml beaker and place this beaker into water bath and maintain the temp.of liquid at 37°C .

Now place one tablet in each tubes. The assembly move up and down at specified rate 30rpm A cylindrical disk made up of plastic is also placed over the Tablet. The disc also generate little pressure on Tablet. Now note the disintegration time

Uncoated tablet: Disintegration within in 15 min.

Sugar coated tablet-within 60 min.

Film tablet-with in 30 min.

Enteric coated tablet-within 60 to 120 min

2.5 .FRIABILITY: Friability test was performed to access the effect of friction and shock which may often cause tablet to chip, cap or break it generally reflects poor cohesion of tablet ingredient. Weighed tablets sample was placed in the chamber and the friabilator was operated for 100 revolution at 25RPM and the tablet were weighed again. Compress tablet should not loss more then 1% of there weight.

Formula = $\frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$

Initial Weight.

2.6 RH: Relative humidity and important factor that effect the quality of pharmaceutical product. It is important humidity in the areas like granulation and compression.

2.7 Temperature: Most of the pharmaceutical activities are done at room temperature (20 to 25°C) is considered room temperature in pharmaceutical.

2.8 WATER ACTIVITY: It is simply defined as the ratio of the vapor pressure of pure water (100% equilibrium relative humidity) to the vapor pressure of the sample. Expressed as 0-100% erh or scaled for water activity in units of 0-1 aW, the effect on the product is easier to understand than the definition. Water activity indicates the free water potential of a product, not the water mass, as a percentage by weight. Although pure water has the highest potential (100% erh saturation or 1.0 aW), interaction with a substance or product lowers the potential and thus lowers the water activity by 1.0 aw. Innovative precision instruments can now measure the water content of a sample at steady state (usually at a precisely controlled temperature) corresponding to the water activity of the product and display the water activity in units of erh or aW with ternary resolution.

2.9 LEAK TEST APPRATUS: Leak testing equipment is a solid state leak testing instrument for food, pharmaceuticals and other industrial chemicals. This instrument is used to check the quality of the packaging process of strips, blisters and bags containing tablets, granules and liquids. It is also used to ensure that the seal surrounding the product is complete.

The device is equipped with a 4-digit bright red LED display based on a 7-segment microcontroller. Soft touch keys provide a comfortable user interface.

The unit has a polycarbonate desiccant housing for long-term vacuum storage. Create high vacuum levels in a short time using a small vacuum pump. A vacuum gauge on the front panel of the instrument indicates the vacuum level. The vacuum gauge is connected to a control valve that disconnects the vacuum in the desiccator from the vacuum source.

The test sample to be analyzed is placed in a polycarbonate desiccator housing. A vacuum pump creates a vacuum in the desiccator. The created vacuum is maintained for a period of time and then manually released. The test specimen to be analyzed must retain its shape during this test, indicating the integrity of the seal. Second, because the test strips/bottles are immersed in a colored dye solution (usually methylene blue). The ventilation in the dryer

allows any hole to pass the paint, and the contents of the flexible packaging are also painted with the same coloring material.

3. RESULT

3.1 MANUFACTURING PROBLEMS OF TABLETS

3.1.1 CAPPING: The partial or complete separation of the top or bottom crowns of a tablet from the Main body of the tablet is termed as capping. Separation of the tablet top from the body is often the result of compressed air, poorly machined or formed dies and punches, misalignment of drive blades, or unnecessarily high turret speeds. Formulation causes of capping defects in tablets are small particles in the granules during compression, improper binding

3.1.2 LAMINATION: Lamination is the separation of a tablet into two more distinct layer. This defect means that the tablet is separated into several layers. This can be caused by excessive turret speed, rapid decompression and increased power. In addition to the rapid loosening of tablet edges due to lack of compressibility of the material, lamination can also result from assembly problems such as lamination

3.1.3 CHIPPING: It is defined as the breakage of tablet edges.

3.1.4 CRACKING: Formation of small, fine cracks on the upper and lower central surface of tablets or very rarely on the sidewall are termed as cracking.

3.1.5 STICKING: The partial or complete separation of the top or bottom crowns of a tablet from the main body of the tablet is termed as capping.

3.1.6 MOTTLING: An unequal distribution of color on a tablet with light or dark on the surface is termed as mottling.

3.1.7 DOUBLE IMPRESSION: It involves only those punches, which have a monogram or other engraving on them. Free rotation of either upper punch or lower punch during ejection of a tablet.

3.1.8 BINDING: These defects are improperly machined dies or molds without proper openings or jagged or rough edges of the tablet due to excessive pressure in the tablet press. Problems with formulations include excessive moisture and other granular factors, as well as insufficient lubrication.

3.1.9 PICKING: If part of the tablet sticks to the punch surface, the main process-related cause is free rotation of the lower and upper punches during tablet ejection or a worn punch surface. Formulation-related selection causes include high pellet moisture content, excessive binder content, and inadequate lubrication.

3.1.10 THICKNESS: Inadequate or inconsistent tablet thickness can be caused by tablet presses that are not properly cleaned or maintained and punching tools that are of different lengths. The main cause related to the formulation is inconsistency in filling the mold.

3.1.11 BLACK SPOT: Contaminated material, burned material in the die opening, and improper feeder placement or adjustment are process-related sources of visible

stains or contaminants on the tablet material. The main cause associated with formulations is contamination in all processes prior to tablet administration. Black spots can also be caused by a unique combination of certain products, car component materials and lubricants.

4. TABLE OF RESULT

Description: An white colour elongated biconvex uncoated	Average weight of tables is 990mg
Punches type/size: 19.60mm 9.00mm	Machin type 27 station
Weight of 20 tablets: 19.404 to 20.196	Average weight of tablet 970 to 1009mg
Thickness 6.20mm	Hardness: NLT 8kgs/cm ³
D.T: NMT 15min	Friability: NMT 1.0% w/w
Area temperature: NMT 25 degree	Area RH: NMT 20%

5. WATER ACTIVITY RECORD

S.NO.	SAMPLE	WATER ACTIVITY	TEMP	RH
1.	Water activity before lubrication	0.037	21.7	12.9%
2.	Water activity after lubrication	0.035	20	13.84%

6. WATER ACTIVITY AFTER COMPRESSION

S.No	Limit	Observation	Temperature	Rh
01	0.060a/w	0.042	21.4 C ⁰	13.2%

7. WATER ACTIVITY AFTER COATING

S.NO.	LIMIT	OBSERVATION	TEMP	RH
1	0.080a/w	0.063	22.4	12.2

COATING PARAMETER

Sr . No.	Parameter	Limits	Sr. No.	Parameter	Limits
1	Pan Speed	20% -30%	9	Cabinet -ve Pressure	Between 5 to 7 mm of Wc
2	Inlet Temperature	50±5°C	10	Spray Rate	Total weight of coating solution of

					three gun should be between 240
				For Gun I	80-100 g/min.
				For Gun II	80-100 g/min.
				For Gun III	80-100 g/min.
3	Outlet Temperature	42±3°C	11	Spray Pattern	Umbrella type
4	Core Bed Temperature	38±3°C	12	Distance between spray nozzle and table surface	7-9 inches
5	Blower / Exhaust	Approx. 50% Approx. 80%	13	RH% of inside coating pan	RH- NMT 10%
6	Atomizing Air pressure	1.5- 2.5Kg/cm ²			
7	Inlet Damper Opening Exhaust Damper Opening	Continuously 'ON'			
8	Fan Air Pressure	1.5- 2.5Kg/cm ²			

CONCLUSION: Based on my research, I found that Amoxicillin and potassium clavulanate tablet fulfilling all the parameters of the ideal tablet i.e. DT, Friability, Hardness, Thickness, water activity. The combination of Amoxicillin and clavulanate acid is used to treat certain bacterial infection like skin infection, lungs infection, urinary tract infection. It will not work for viral infection such as common cold.