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Formulation and Evaluation of Amoxycillin and Potassium Clavulanate Combination Tablet with Tabsafe MB as Coating Material as Compared to Instacoat Sol White as Coating Material

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ABSTRACT

Tablet coating generally refers to the application of coating material whether aqueous, non-aqueous, sugar or any other coating material as its outer coat for various beneficial results. Among these masking of odor, masking of taste, minimizing incompatibility, physical & chemical protection, increasing mechanical strength, to protect during transportation, good looking also comes. This research is based on the film coating of the most generally used antibiotic combination tablet namely Amoxycillin TH and Potassium Clavulanate tablet. Amoxycillin and Potassium clavulanate tablets are oral antibiotic dosage forms containing Amoxycillin as a semisynthetic antibiotic and Potassium clavulanate as a B-lactamase inhibitor. The universally used coating material for its protection against the atmospheric condition of temperature, pressure, and transportation is Instacoat sol white. In this research Tabsafe MB as coating material protection and compatibility with this formulation has been illustrated with third-month stability results and the conclusion is that Tabsafe MB as coating material can be also used and works even better than Instacoat sol white as coating material. The instrumental analysis along with in vitro drug release with chromatographic analysis was done to check its results for better pharmacological effect. The formulation of the tablet and the unit operation performed at each step is briefly taken into account for a full understanding of the research topic. While primary packaging and desiccants are considered a dosage form's most significant defense from the environment, specialized film coatings such as Opadry Amb II can provide further moisture protection, as demonstrated in the case study below. Film coatings can protect sensitive compounds from temperature and humidity excursions before packaging including instances of bulk product storage, transport, or repackaging. In-use product integrity testing ensures the product quality before or after removal from primary packaging during temperature and humidity excursions, bulk storage, transport, or repackaging. There is often limited consideration given to storage conditions when the dosage form has been dispensed by the pharmacist, caregiver, or patient. Film coatings help to protect the integrity of the dosage form when removed from the primary packaging. Coating material for the production of AMXCV Tablet: Opadry white OY-C-7000A of Colorcon company Hypromellose (HPMC) based film coating is generally done for AMXCV Tablet. But Tabsafe Moisture Barrier is being used in this formulation and for comparative study instacoat sol white as the coating material is used which is also one of the better coating materials which has been widely used.

INTRODUCTION

Tablet coating simply refers to a process of applying coating solution onto the outer surface of a solid dosage form to acquire various benefits like:

- masking of odor
- masking of taste
- to minimize incompatibility
- for physical & chemical protection
- to increase mechanical strength)
- to protect during transportation
- to make sustain release or controlled-release tablet

Tablet coating solvent: The k-30 is commonly used as a binder and coating formulation for tablets as it has excellent solubility when it is mixed with water, intestinal fluid, gastric and even organic solvents.

The novelty of this project is stated below:

Coating material for the production of AMXCV Tablet: Opadry white OY-C-7000A of Colorcon company Hypromellose (HPMC) based film coating is generally done for AMXCV Tablet. But Tabsafe Moisture Barrier is being used in this formulation and for comparative study instacoat sol white as the coating material is used which is also one of the better coating materials which has been widely used.

Tab Safe MB" may be defined as customizable, pre-blended coating material without a plasticizer, which has the ability to add specific plasticizers to achieve individual market needs. Available in a variety of polymers, "TabSafe MB" helps to lesser inventory and raw material testing. TabSafe MB" can be understood as customizable, pre-blended coating material without a plasticizer, which possesses the ability to add specific plasticizers to meet individual market requirement. It is available in a variety of polymers,

In Moisture Barrier coating, water-insoluble material is used to prevent the diffusion of water vapor across coated tablets. Stearic Acid, Ethylcellulose, and Metacryclic Acid Copolymers

have commonly used materials that have the property of diffusing moisture vapor transmission but due to their water-insoluble nature, it takes more time to disintegrate.

Tabsfe MB is a perfect combination of plasticizers, pigments, pacifiers, and other excipients which is compatible with organic or hydroalcoholic systems to protect against atmospheric moisture. In addition, disintegration or dissolution time is not impacted by our MB coating.

Impact of Moisture Barrier Film Coating on Stability of Amoxicillin/Clavulanic Acid Tablets

Product stability is affected by all elements of solid dosage development and manufacturing which include core formulation, choice of excipient, production conditions, packaging, and storage conditions, it reaches to consumer hand. Coating provides stability to the tablets in handling, transporting and prevents them from sticking together. The coating also improves the mechanical strength of the dosage form, causes the dosage form smoother at outer surface and more suitable for swallowing purposes to patient (increase patient compliance). Pharmaceutical companies print their marks, symbols, or abbreviations on the tablets and mask a disagreeable color or odor of the tablets and leave company image for marketing. The release of the active ingredient can even be controlled with the help of coatings very easily. Coated dosage forms could be site-specific which act at a specific receptor. The coating prevents acid-sensitive drugs from having a negative impact on the intestine. The drug release rate in the gastrointestinal tract (GIT) could be controlled by controlling the dissolution rate of the tablet.

Amoxicillin and clavulanic acid are combined which has action against some amoxicillin-resistant bacteria. Due to the high sensitivity of clavulanic acid to moisture, this combination was selected to investigate the moisture protection properties of Tabsafe MB. This antibiotic combination product is typically coated with a hypromellose (HPMC) based film coating but here the universal Instacoat Sol white and Tabsafe MB is chosen as a coating material.

- Description: Amoxycillin and Potassium clavulanate tablets are an oral antibiotic dosage form containing Amoxycillin as a semisynthetic antibiotic and Potassium clavulanate as:
- B-lactamase inhibitor
- Clinical Pharmacology: Well absorbed from GIT after oral administration

- Indications: In the treatment of infection caused by certain strains of bacteria in the condition of the disease like Respiratory tract infection, UTI, Otitis, malaria, and skin infection.
- The coating material used: Tabsafe MB, Instacoat Sol White.

Things that have been planned to carry out the project under this topic:

- Preformulation studies
- Formulation of tablet
- Evaluation of tablet
- wt. variation
- Hardness
- Friability
- Thickness
- Disintegration test
- Uniformity of content
- In vitro Release studies

INSTRUMENTAL ANALYSIS:

Almost all analytical instruments are electrically operated by user. An understanding of the operation of the electrical components of an instrument can aid in locating a malfunctioning portion of the instrument and can make it possible for the analyst to obtain maximal use and information from the instrument.

Analytical instrument are those devices which measure physical or chemical property of the drug substance or that measure some parameters that makes determination of a property of the substance easier. Previously, instrumental analyses were divided into three categories as per the requirement of the type of property of the assayed substance that need to be measured. They are:

1. Spectral Methods – This method use or measure some sort of radiation absorbed or reflected by sample molecule during the assay.

2. Electroanalytical Methods- This method applies an electrical signal to the sample and /or monitor an electrical property of the sample at electron motion level.

3. Separative method- This method depends upon separation of the components of a sample before measuring a property of the components in a mixture of two or more components.

SPECTRAL METHODS:

The spectral method of analysis uses an instrument to measure the amount of radiation that is absorbed, emitted, or scattered by the sample.

If the amount of absorbed radiation is measured, the technique is absorptiometry or absorption spectrophotometry.

Except for naturally occurring radioactive material, radiation can be emitted from a sample only after the sample has absorbed energy from some outside source. If the absorbed radiation is electromagnetic radiation in the X-ray, UV, or visible region of the spectrum, the subsequently emitted electromagnetic radiation is a form of luminescence termed either Fluorescence or Phosphorescence depending upon how deexcitation takes place.

Radiation which is being scattered from sample molecules can be used for analysis. The examples of analytical techniques that rely upon scattered radiation are Nephelometry, turbidimetry, and Raman scattering.

The ratio of the speed of electromagnetic radiation in a vacuum to the speed of radiation of the same wavelength in a sample is the Refractive index of the sample. The RI is usually determined by measuring the extent to which the direction of travel of the radiation is altered as it enters the sample. Because the RI is a characteristic of a substance, refractometry definitely has application that can be used for analysis.

ELECTROANALYTICAL METHODS:

These instrumental method of chemical analysis in which either an electrical signal is applied to one of the electrodes dipping into the sample solution or an electrical property of the solution is measured are the electro analytical method.

Most electroanalytical method apply an electric signal in which atomic sub particles motion is monitored while a different electrical parameter of the solution can be measured.

Various types of electroanalytical methods:

1. Amperometry
2. Potentiometry
3. Conductometry
4. Coulometry
5. Voltammetry
6. Electrogravimetry

SEPARATIVE METHOD: The separative method takes advantage of the physical or chemical properties of the component of a mixture to separate the components. After the separation, each of the components can be individually assayed either qualitatively or quantitatively as per requirement. Nowadays, the separating instrument online performs the separation and the sassy. In other cases, the separation is done before an assay by the method.

The instrumental separative techniques are divided as:

1. Chromatography
2. Electrophoresis
3. Mass spectrometry

1. Chromatography: this is the method by which a mixture is separated into its components as a result of the ability of each component to be flushed along or through a stationary phase by a mobile phase. The sample is placed on the edge of the stationary phase (a solid or liquid) and a mobile phase (a liquid or gas) is allowed to flow over the stationary phase and to sweep the sample along the length of the stationary phase. Components that move strongly and attaches to the stationary phase are swept with less rate across the length of the stationary phase than are those components that less strongly adhere to the stationary phase. The result is a separation of sample components in space at a fixed time after the start of separation or a separation at specified time at a fixed distance along the length of the stationary phase. Chromatography is divided into Liquid and Gas Chromatography depending on the state or nature of the mobile phase.

METHOD OF FORMULATION

Formulation		QTY in Gm					
		P1	P2	P3	P4	P5	P6
Purimox compacted -P (Amoxicillin T/H)*	IP	181.201	181.201	181.201	181.201	181.201	181.201
Potassium Clavulanate Mixture with MCCP 102(1:1) eq. to Clavulanic acid**	IP	103.501	103.501	103.501	103.501	103.501	103.501
pregelatinized starch	IP	18	22	18	24	0	38
mccpph 112	USP	20	20	24	20	38	0
crosspovidone		6	6	6	0	6	6
Ssg	IP	4	4	0	4	4	4
Ccs	IP	4	0	4	4	4	4
mg sterarate	Ip	2	2	2	2	2	2
talc	Ip	3	3	3	3	3	3
Aerosol	IP	3	3	3	3	3	3
	Total	344.702	344.702	344.702	344.702	344.702	344.702
Coating Material							
Instacoat Sol white	IHS	15	15	15	15	0	0
Tabsafe MB	IHS	0	0	0	0	15	15
Isopropyl Alcohol	IP	100	100	100	100	100	100
Methylene Chloride	BP	180	180	180	180	180	180

Process:

1) **Sifting**: Pass the MCCP 112 and Starch through #30 mesh. Pass Crospovidone, SSG, CCS, and Aerosil 200 through #60 mesh. Transfer the sifted excipients into an octagonal blender and mix for 5 minutes.

2) **Drying**: Dry MCCP 112 and Starch, Mg stearate and P. Talc in a Tray drier at 50-60°C for 2 hours.

Addition of API: Sift Purimox compacted –P through #20 & Potassium Clavulanate through # 30 and transfer them to the octagonal blender and mix it with the above dry mixed bulk for 15 minutes (forward and backward direction).

1) **Lubrication**: Sifting of Magnesium stearate and Purified Talc through #60 mesh. Transfer it to the above dry mixed bulk and mix for 5 minutes.

Compression And Coating: After fixing hardness and specific punch die with a specific limit for dimension, the tablets are compressed and the coating solution is coated for the final coated sample analysis

S. No.	PARAMETER	STANDARDS
1	AVERAGE WEIGHT OF TABLET	**1150 mg**
2	WEIGHT OF 20 TABLETS	23.00 g
3	WEIGHT VARIATION OF 20 TABLETS	± 3 %
4	HARDNESS	NLT 3.0 Kg/cm^2
5	THICKNESS	**6.2 ± 0.2mm**
6	FRIABILITY	NMT 1 %
7	DISINTEGRATION	NMT 10 min

A sampling of coated tablets for QC test

Analysis of formulated tablet as per the above formula stated and successive evaluation of tablet as per the stated parameters to verify the success or failure of the formulation and to compare which of the formulation is better for the drug release to give its antibiotic pharmacological effect.

The Quality control test is done for all 6 formulations. The 1st four formulations are not stable but the last 2 formulations namely 4th (Instacoat Sol white as coating material) and 6th formulation (Tabsafe MB as coating material) are stable and further comparative studies are done to choose the better option.

The 1st formulation was studied and was found that the assay of clavulanic acid is around 99% and the disintegration time was found to be 55 minutes which is not satisfactory as it has a high degradation rate so it will not be stable to provide the required therapeutic effect after

a short period. So it was further modified in some aspects as stated above in the tabular form of formulation as 2 formulations and the quality test is performed. In the 2nd formulation, the assay of Amoxycillin TH is outside the limit so further 3rd formation was undertaken to evaluate. In the 3rd formulation, the Amoxycillin TH Assay is not as much as expected to give its pharmacological action. So 4th formulation was done to investigate for good results. Fortunately, this formulation was good and had been coated with Instacoat sol white everything was repeated in the 5th formulation and coated with tab safe MB but the formulation was not good as expected so it was modified as the 6th formulation, and results show good outcomes.

Now, further study is being done for comparative study for instacoat sol white and tab safe MB as a coating material in a generally prescribed combination of antibiotics namely Amoxycillin TH and potassium clavulanate.

HPLC Method was chosen for study with dissolution test apparatus according to Indian Pharmacopeia monographs.

CONCLUSION

Sl.No.	**Formulation**	**Assay (Initial)**	**After 3 Months (Real Time Stability)(Temperature:25±2°C,RH75±5%)**		
		Amoxycillin TH	**Pot. Clavulanate**	**Amoxycillin TH**	**Pot. Clavulanate**
1.	1st	101.35%	99.39%		
2.	2nd	135.44%	100.70%		
3.	3rd	88.31%	121.80%		
4.	4th	99.77%	116.41%	98.68%	109.36%
5.	5th	104.44%	115.21%		
6.	6th	106.85%	118.06%	106.44%	117.33%

Hence, it is concluded that Tabsafe MB as a coating material can give better protection and pharmacological effect as compared to that Instacoat Sol white as a coating material.

Impact of Moisture Barrier Film Coating on Stability of Amoxicillin/Clavulanic Acid Tablets

Product stability is mostly affected by all elements of solid dosage development and production including core formulation, excipient choice, manufacturing conditions, packaging, and end-use storage conditions. The film coating has ability to protect tablets from environmental factors such as moisture, light, or oxygen while presenting the opportunity to improve product identification and patient compliance.

The impact of Moisture Barrier Film Coating on the Stability of Amoxicillin/Clavulanic Tablets was studied.

Amoxicillin and clavulanic acid are general antibiotic with an increased spectrum of action against some amoxicillin-resistant bacteria. Due to the high sensitivity of clavulanic acid to moisture, this combination was selected to investigate the moisture protection properties of Tabsafe MB. This antibiotic combination product is typically coated with a hypromellose (HPMC) based film coating but here the universal Instacoat Sol white and Tabsafe MB is chosen as coating material.

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