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Review Article

Assessments of active pharmaceutical ingredient and excipients in some pharmaceutical formulations

Ahmed Jassim Muklive Al-Ogaidi[1*], Firas Al-Oqaili[1], Liblab S. Jassim[1], Shaymaa S. Hassan[1], Hamssa Ahmed Easa[1]

[1]The University of Technology, Iraq.

ABSTRACT

Active Pharmaceutical Ingredient is a substance that considered as one of the important materials that enter into the manufacture of the final pharmaceutical product, and its activity. Pharmaceuticals have a significant impact on the treatment and diagnosis of pathological conditions, and thus reduce the economic burden of the disease. As well, it has a role in the restoration, correction, or modification of physiological functions in human. Excipients play an important role in a drug's performance, including bioavailability, improving solubility, preserving the PH, stability, and determining the profile of the release. The reduction in the production cost of active pharmaceutical ingredient is not only due to the reduction in workers' wages, beside to innovations in the production method, which could help to reduce the economic state. The excipients have an essential part in industry of drugs, which contain a dependable, repeatable production method that produces a more stable product over time and increasing patient compliance.

Keywords: Active pharmaceutical ingredient, amoxicillin drug, cephalexin drug, excipients.

INTRODUCTION

Active Pharmaceutical Ingredient

Active Pharmaceutical Ingredient (API) is considered as one of the important materials that enter into the manufacture of the final pharmaceutical product, and its activity Pharmaceuticals have a significant impact on the treatment and diagnosis of pathological conditions, or in the restoration, correction, or modification of physiological functions in humans [1].

It is possible to see the following notes on the medicine packaging, for example, the quantity and name of the substance that sometimes does not require a prescription [2].

The API is the most important component of any medicine; nevertheless, The physical and chemical properties of most APIs are lacking traits required to produce a medicine on their own Consequently, a types of pharmaceutical ingredients are available or being created to aid in the creation of products and processes for transforming drug substances to the final process of drug production.

Excipients have an essential part in a drug's production, including bioavailability, improving solubility, preserving the PH, stability, and determining the profile of the release. Changes that occur in chemical and physical properties can have an impact on the drug production process.

While the most significant factor to product cost is the API cost of any formulation, the excipients employed in drug process formation can also make a considerable contribution [3]. Excipients are becoming more important as drug product manufacturers explore for ways to save costs beyond the API.

Excipients are becoming an increasingly popular way to cut costs nowadays, despite the fact that they have not traditionally been a key driver of cut costs.

*Correspondence: Ahmed Jassim Muklive Al-Ogaidi , The University of Technology, Iraq. email: ahmed.mukleef@yahoo.com
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There are two ways: the first method depends on modifying the excipients that are actually used in order to help increase the purchase of the medicinal product.The second depends on finding new excipients that are from other sources and have a lower cost [4], and the second depends on finding new excipients that are from other sources and have a lower cost.

Other considerations, in addition to the cost, may affect a company's decision to replace its present material source. These include the following: Having a variety of sources, intellectual property protection, current supplier's quality [5].Active ingredients in some drugs could be illustrated in Table 1.

Excipients

Components of drug products known as an Excipients, with the kind and number of excipients varying by depending on the dosage form. While the API is responsible for the drug product's therapeutic impact, the excipients play an important role in the formulation in production of drug [9]. Which contain a dependable, repeatable formation method that produces more stable drug compound. The benefit of excipients are increasing patient compliance, enable/improve bioavailability and consistency, controlling medicine delivery, homogeneous mixing of drugs, make the taste more acceptable, especially for children [10]. In Table 2, excipients in Tamsulosin, Cephalex and Amoxil are illustrated.

Table 1. Active ingredients in some drugs

Drugs	Active ingredients	Active ingredient form	Solubility
Tamsulosin [6]	Tamsulosin hydrochloride	White crystalline powder	It is soluble in water, soluble in formic acid, and less soluble in aqueous ethanol.
Cephlex [7]	Cephalexin mono hydrate	White powder	Soluble in water
Amoxil [8]	Amoxicillin tri hydrate	White powder	Soluble in water

Table 2. Pharmaceutical excipients in some drugs.

Drugs	Pharmaceutical Excipients
Tamsulosin	Meth acrylic acid copolymer, microcrystalline cellulose, calcium stearate, titanium dioxide, ferric oxide , isopropyl alcohol, propylene glycol [11].
Cephlex	Sodium saccharin, Sodium Benzoate,Magnesium Stearate, Sucrose, Car boxy methyl cellulose, Raspberry.
Amoxil	flavor, Pineapple flavor [12]

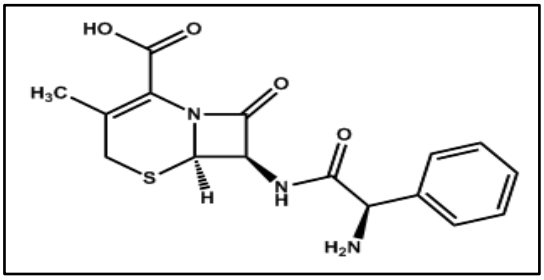

Figure 1. The structure of cephalexin [14]

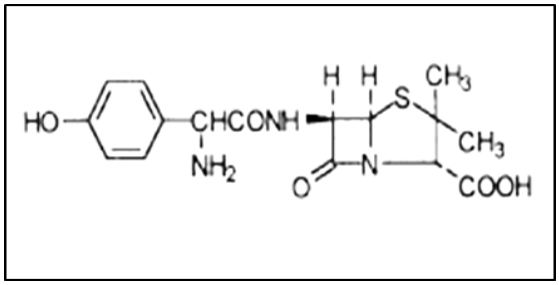

Figure 2. Structure of Amoxicillin [20].

Cephalexin Drug

Cephalexin belongs to the beta -lactam antibiotic family [13]. It's chemically referred to as (6R,7R)-7-[[(2R) -2-Amino-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate. Cephalexin has the molecular weight of 365.4 and the chemical formula C16H17N3O4S. H2O.

The Figure1, show the structure of cephalexin. It is treatment of certain bacterial infections such as respiratory tract infections, otitis media, and urinary tract infections. It is bactericidal and inhibits the peptidoglycan layer of the bacterial cell wall by binding irreversibly to the active site of PBP, which is required for cell wall formation [15].

Cephalexin is acid-stable and can be taken with or without food. Following oral administration, it is readily absorbed. At 1 hour after dosages of 250 mg,500 mg, and 1 g, average peak serum concentrations of 9, 18, and 32 g/mL were achieved, respectively [16].

By glomerular filtration and tubular secretion, cephalexin is eliminated in the urine [17]. Moreover, Cephalexin is a powder that ranges from white to a pale yellow color, water soluble to a degree, insoluble in ethanol , chloroform and ether [18].

Amoxicillin Drug

Amoxicillin is the phydroxy counterpart of Ampicillin, a semi-synthetic Penicillin that was first marketed in 1974. (Sciencedirect 2007). 6-APA (6-aminopenicillanic) is acylated with p-hydroxyphenyl glycin to produce it. It's an antibiotic with a wide range of bacterial activity that's used to treat a variety of Gram-positive and Gram-negative bacteria.

It has an identical antibacterial 17 spectrum to Ampicillin, and it is resistant to acids, susceptible to alkaline and -lactamase hydrolysis, and weakly protein bound [19].It is chemically (2S, 5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl) acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid and has the following structure Figure 2.

It is a widely used antibiotic in human and veterinary medicine for the treatment and control of respiratory, gastrointestinal, urinary and skin bacterial infection. Due to its pharmacological and pharmacokinetic properties caused by Gram-negative and Gram-positive bacteria , it is used to treat infections of the middle ear (otitis media), urinary tract ,throat, larynx (laryngitis), pharynx (pharyngitis),bronchitis, and lungs (pneumonia).

It was marketed in 1972 and still remains the most commonly utilized drug in this class because its oral absorption is better when compared with other ß -lactam antibiotics [21].It works against germs by preventing the formation of bacterial cell walls. Amoxicillin prevents the crosslinking of linear peptidoglycan polymer chains, which are a significant component of the bacterial cell wall [22].

Additionally, it's a crystalline white powder, It's odorless and tasteless in practice, It's only a smidgeon soluble in water, Ether, chloroform, and fixed oils are practically insoluble, It dissolves in alkali hydroxide solutions that are dilute [23].

Some microorganisms, such as those that produce penicillinase, are resistant to the antibiotic Amoxicillin (particularly penicillinase producing staphylococcus sppetc). Amoxicillin, on the other hand, has been demonstrated to remove resistant germs when the dose is increased [24].Amoxicillin comes in three forms: trihydrate capsules and syrups for oral use, and sodium salt for

intravenous treatment [25]. Differences between cephalexin and amoxicillin drugs are illustrated in Table 3.

Antibiotics with the β-lactam (a four-membered cyclic amide) ring structure are the most often used antibiotics for the treatment of bacterial illnesses today [28]. β-lactam antibiotics are a type of broad-spectrum antibiotic that includes all antibiotics with the following common [29] molecular structure: The -lactam is a four-atom ring. Penicillin is the most commonly given antibiotics [30].

Antibiotics with a -lactam ring, a four-sided structure with three carbon atoms and one nitrogen atom, are known as -lactam antibiotics. Hermann Staudinger created the first synthetic -lactam ring system in 1907 [31].

β-lactam antibiotics classified into [32]: Penicillin, Cephalosporin, Carbapenems Monobactams , Ampicillin, Amoxicillin [33].

Table 3. Differences between cephalexin and amoxicillin

Cephalexin	Amoxicillin
One of the medicines used to treat a wide range of diseases, from the first generation beta-lactam antibiotics [26].	It is considered a penicillin antibiotic and at the same time a beta-lactam antibiotic. It will prevent the formation of the cell wall and thus lead to cell death [27].

Table 4. Types of drug stability[38]

Stability type	Conditions maintained throughout the shelf-life of the drug product
Chemical state	According to limitations, each active component maintains its chemical integrity and declared potency.
Physical state	The look, palatability, uniformity, dissolution, and suspend ability of the original physical attributes are preserved.
Microbiological state	That are present maintain their efficacy within the limitations set.
Therapeutic type	The therapeutic impact is the same.
Toxicological state	Significant increase not present

Dry Powder of Oral Reconstitutable Suspension

Oral suspension made from dry powder that can use right away. A significant category of suspensions necessitates mixing prior to administration. These dry formulations must be diluted with water before being dispensed. If stored at refrigerator temperatures after reconstitution, these systems have a short but acceptable life [34].

Reconstitutable oral systems demonstrate acceptable chemical stability of the medicine over time, eliminate physical stability issues such as solubility, PH, and incompatibility with other constituents, and lower drug costs because the aqueous carrier is not present, the finished product's weight may be lowered, and thus transportation costs may be reduced.

The drug is delivered in dry form since it may be stored for a long period in dry form but deteriorates quickly in solution. The shelf life of such a solution is said to be short [35].

The chemical stability of the active substances can maintain until reconstitution at the commencement of therapy with a reconstitutable suspension. By adjusting the volume to swallow,

the same suspension can easily give to children of various ages [36].

Stability Study

We can refer to stability as the range or period in which the product can maintain the properties and advantages that were present during the manufacturing period.

There are five types of stability. Alternatively, it is a pharmaceutical product's capacity to maintain its qualities within prescribed limitations over the course of its shelf life.

The following factors of stability should take into account: biopharmaceutical, chemical, physical, microbiological, and chemical [37].

Types of stability study could be explained in Table 4. In certain cases, drug instability in pharmaceutical formulations can be recognized by changes in the formulation's.

To examine the stability of a formed product, it is common to subject it to high stress conditions in order to accelerate its deterioration and so shorten the testing period.

This allows for more data to be collected in less time, allowing for the early elimination of unsatisfactory formulations and a reduction in the time it takes for a successful product to reach the market [39].

Conclusion

Active Pharmaceutical Ingredient is considered one of the important materials that enter into the manufacture of the final pharmaceutical product, and its activity Pharmaceuticals have a significant impact on the treatment and diagnosis of pathological conditions, or in the restoration, correction, or modification of physiological functions in humans.

Excipients play an important role in a drug's performance, including bioavailability, improving solubility, preserving the PH, stability, and determining the profile of the release increasing patient compliance.

Moreover, enable/improve bioavailability and consistency, controlling medicine delivery, homogeneous mixing of drugs.

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Conflicts of Interest

We have no conflicts of interest to disclose.

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