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A REVIEW OF ANALYTICAL METHODS FOR ESTIMATION OF AMOXICILLIN TRIHYDRATE AND TINIDAZOLE IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Amoxicillin, an acid stable, semi-synthetic drug belongs to a class of antibiotics called the Penicillins (beta-lactam antibiotics). It is shown to be effective against a wide range of infections caused by wide range of Gram -positive and Gram- negative bacteria in both human and animals. Tinidazole is a prodrug and antiprotozoal agent. Both the drugs are used to treat Gastro intestinal infectious diseases and upper respiratory tract infections. Techniques like UV-Visible spectrophotometry, potentiometry, High Performance Liquid Chromatography (HPLC), High performance Thin Layer Chromatography (HPTLC) *etc* have been used for analysis. UV-Visible spectrophotometry and HPLC methods have been used most widely.

KEYWORDS

Amoxicillin, Tinidazole, UV-Visible spectrophotometry, HPLC and HPTLC.

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INTRODUCTION

Amoxicillin (α-amino hydroxyl benzyl penicillin) is a semi synthetic antibiotic, belonging to the β Lactam family, which is effective for bacterial infection treatment, especially for *Helicobacter pylori* infection. Chemically Amoxicillin is (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. The chemical structure is shown in Figure No.1. Amoxicillin trihydrate acts by inhibiting the cross-linkage between the linear peptidoglycan polymer chains of the cell wall of gram positive bacteria such as *Streptococcus spp*., *Staphylococcus. spp.* and *Enterococcus spp.* and gram-negative organisms such as Haemophilus,

Neisseria, Escherichia, Proteus and *Salmonella spp*[1].

Tinidazole is a 5- nitroimidazole derivative, an antiparasitic drug used against protozoan diseases. It is used in the treatment of variety of amoebic and parasitic infections. It is chemically 1-(2 ethylsulfonylethyl)-2- methyl-5-nitro imidazole[2]. The chemical structure is shown in Figure No.2. Both the drugs are used to treat Gastro intestinal infectious diseases and upper respiratory tract infections. Number of methods have been reported for estimation of Amoxicillin and Tinidazole individually or in combination with other drugs.

In the present work, we have reviewed some of the recently published analytical methods for Amoxicillin and Tinidazole. Analytical method development and validation play important roles in the discovery, development and manufacture of pharmaceuticals. Analysis of drug is important to ensure high efficacy and safety for patients. Analysis of Tinidazole tablet formulation by the Indian Pharmacopoeial (IP) method is performed by spectrophotometry. Besides this, various other methods reported for the analysis of Tinidazole include gas-liquid chromatography (GLC), spectrophotometric assay, thin layer chromatography, high pressure liquid chromatography and the electrochemical method based on single-wall carbon nanotubes, direct current (DC) polarography and differential pulse (DP) polarography. British Pharmacopoeia describes potentiometric and nonaqueous titration methods using perchloric acid as a titrant[3]. For the analysis of amoxicillin in pure form and in pharmaceutical formulations Pharmacopoeias have reported liquid chromatography and potentiometric methods.

ANALYTICAL METHODS FOR ESTIMATION OF AMOXICILLIN AND TINIDAZOLE

UV Visible spectrophotometry

Some UV-Visible spectrophotometric tests have been developed to quantify Amoxicillin and Tinidazole in pharmaceutical formulations. Spectrophotometric method for amoxicillin is based on the formation of coloured (charge transfer or ionpair) complex between drug and reagent which can be estimated by visible spectrophotometry[4]. In some studies other than original spectrophotometric studies, derivative spectrophotometric methods are used. These include first and second order derivative UV spectrophotometry. Direct UV spectrophotometric study is carried out in case of Tinidazole. The UV spectrophotometric studies reviewed are summarized in the Table No.1.

Potentiometry

Potentiometry is the field of electro analytical chemistry in which potential difference is measured under the conditions of no current flow. The measured potential may then be used to determine the analytical quantity of interest, generally the concentration of some component of the analytic solution. Studies show that potentiometric titrations are also used for the analysis of Amoxicillin and Tinidazole. Amoxicillin in buffer is titrated with mercuric nitrate[5] and Tinidazole in acetic acid is titrated with perchloric acid and end point being determined potentiometrically[6].

CHROMATOGRAPHIC METHODS

High -Performance Liquid Chromatography (HPLC)

HPLC is an advanced form of liquid chromatography used in separating the complex mixture of molecules encountered in chemical and biological systems, in order to recognize better the role of individual molecules. HPLC is an analytical tool which is able to detect, separate and quantify the drug, its various impurities and drug related degradants that can form on synthesis or storage. It involves the understanding of chemistry of drug substance and facilitates the development of analytical method. A number of chromatographic parameters were evaluated in order to optimize the method. An appropriate mobile phase, column, column temperature, wavelength and gradient must be found that afford suitable compatibility and stability of drug as well as degradants and impurities. Among the chromatographic techniques HPLC has been the most widely used system. HPLC. Table No.2 describes the summary of the chromatographic methods used for analysis of

amoxicillin and tinidazole as individual drugs or as combinations, with the method description.

High Performance Thin Layer Chromatography (HPTLC)

With the advancement of the technique, high performance thin layer chromatography (HPTLC) emerged as an important instrument in drug analysis. HPTLC is a fast separation technique and flexible enough to analyze a wide variety of samples. This technique is advantageous in many means as it is simple to handle and requires a short analysis time to analyze. It is suitable for both qualitative and quantitative analysis. High performance thin layer Chromatography is used for analyzing tinidazole but it is not used widely for analyzing Amoxicillin. Chromatographic method is summarized in Table No.3.

Table No.1: UV-Visible spectrophotometric methods

DRUGS	S.No	Method	Solvent	λmax (nm)	Linearity (µg/ml)	% Recovery	Reference
Amoxicillin	1	Zero order UV spectrophotometry	0.1 NaOH	247	3.2-48.0	99.67	7
	2	First order UV spectrophotometry	0.1 NaOH	255.8	3.2-48.0	99.04	7
	3	Second order UV spectrophotometry	0.1 NaOH	249.2	3.2-48.0	99.43	7
Tinidazole	4	Direct UV visible spectrophotometry	0.5 NaOH	368.6	20-150	99.86	8

Table No.2: HPLC methods reported for the estimation of amoxicillin and tinidazole

S.No	Drug	Column	Mobile Phase (V/V)	Detector Wavelength (nm)	Flow Rate (mL/min)	Reference
1	Amoxicillin	C18 4.6mm x 15cm	ACN: phosphate buffer (5:95v/v)	230	1.0	9
2	Tinidazole	Hypersil ODS C_{18}	ACN – 0.1% phosphoric acid	316	1	6
3	Tinidazole and Ciprofloxacin	Aligant Zorbax Rx-C_{18} 150 x 4.6mm	Ortho -phosphoric acid: methanol(70:30%v/v)	225	1.5	10
4	Amoxicillin – Tinidazole	Luna C_{18} 250 x 4.6mm	Potassium dihydrogen orthophosphate: CAN (40:60%v/v)	238	1	11
5	Amoxicillin Trihydrate – Tinidazole	Hiq Sil C_{18} 250 x 4.6mm	Disodium hydrogen phosphate :ACN (30:70%v/v)	240	1	12
6	Ofloxacin – Tinidazole	Kromasil C_8 15cm x 4.6mm	Triethylamine: CAN (73:27%v/v)	303	1.2	13
7	Amoxicillin – Flucloxacillin	Kromasil C_{18} 250cm x 4.6 mm	Potassium dihydrogen orthophosphate: CAN (75:25%v/v)	225	1.5	14

Table No.3: Chromatagraphy methods- High Performance Thin Layer Chromatography (HPTLC)

S.No	Drugs	Stationary phase	Mobile phase	Detection	Reference
1.	Clotrimazole-Tinidazole	Aluminium backed silica gel 60	Toluene: Ethyl Acetate: methanol: triethyl amine	220nm	15

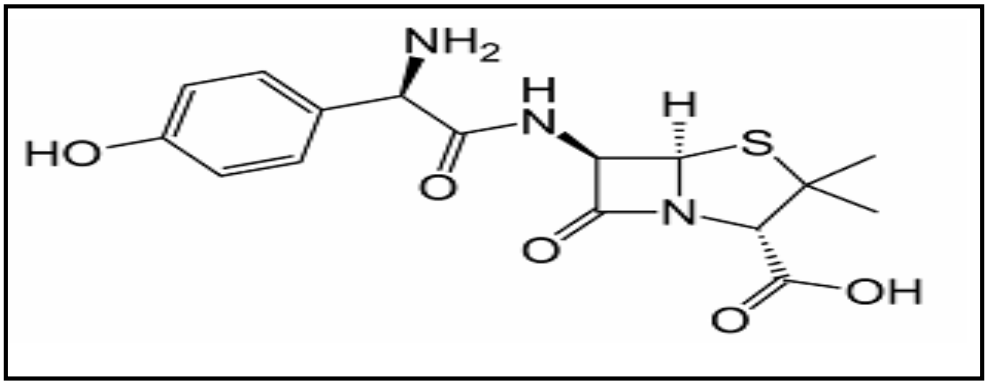

Figure No.1: Chemical structure of Amoxicillin

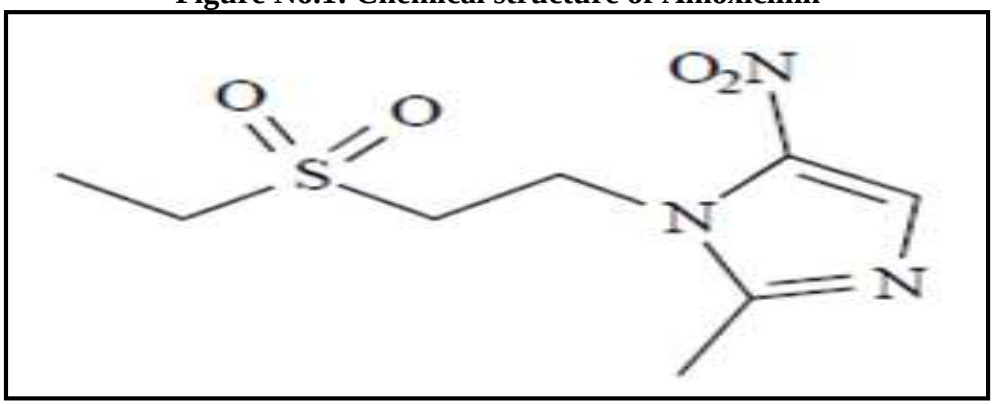

Figure No.2: Chemical structure of Tinidazole

CONCLUSION

The presented review highlights on various analytical methods reported on Amoxicillin and Tinidazole individually and in combination with other drug. UV-Visible spectrophotometry, HPLC, HPTLC, Potentiometry etc were used for the analysis of Amoxicillin and Tinidazole. Among these, HPLC-UV methods were found to be most widely used. HPLC method is frequently used because of high sensitivity, specificity and better separation efficiency. These chromatographic methods are rapid and far more economical. The presented information is useful for the researchers.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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