Review on spectroscopic analytical methods for determination of metformin hydrochloride

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Abstract

Simple sensitive methods to estimate the metformin hydrochloride. It works to reduce blood glucose level in NIDDM patients. Metformin is a biguanide anti hyperglycemic agent. It works by decreasing glucose production by the liver and increasing the insulin sensitivity of body tissues. Literature survey reveals analytical methods such as UV Spectrophotometry, liquid chromatography, gas chromatography, GC-MS, flow injection fluorescence and flow injection MS/MS, have been reported for estimation of the metformin hydrochloride in pharmaceutical formulations and biological fluids.

Keywords: Metformin, Analytical methods, liquid chromatography

1. Introduction

Metformin hydrochloride, chemically 1, 1-dimethyl biguanide hydrochloride is a white crystalline powder, hygroscopic and freely soluble in water, used as a hypoglycemic drug: molecular formula C₇H₁₁N₃HCl [1-2] structural formula of metformin drug show in figure 1. The name "Metformin" is the BAN, USAN and INN for the medication. It is offered beneath a number of trade names, which include Glucophage XR, Carbophage SR, Riomet, Fortamet, Glumetza, Obimet, Gluformin, Dianben, Diabex, Diaformin, Siofor, Metfogamma and Glifor. It is used as an antihyperglycemic (antihyperglycemic) and for the treatment of kind 2 diabetes according to the World Health Organization (WHO) which often influences those over the age of forty years as properly as in addition to extraordinary age agencies induced by insulin deficiency due to the presence of weakness in the beta cells) in The pancreas, which secretes insulin or as an end result of the introduction of sites in the body, or because of insufficient resistance to insulin receptors, especially in humans with weight problems [3-7] considering it works to counter insulin resistance, in particular in the liver and skeletal muscles, and increases the sensitivity of the insulin surrounding in some tissues Like muscles, and tissues Lipomas works on the oxidation of fatty acids and promotes decomposition of peripheral glucose [8-10]. Metformin was once first synthesized in the 1920, because of a want for a drug that diminished blood sugar levels. After that, he disregarded this drug for two decades, with research pastime in insulin and other anti-diabetic drugs. Then manufacturing of metformin flourished in late 1940, after various reports proved that it may want to lead to low blood sugar. In 1957, the French medical doctor Jean Stern, published the first clinical trial of metformin as a therapy for diabetics. It was produced in the United Kingdom in 1958, in Canada in 1972, and in the United States in 1995, and it is believed to be the most extensively prescribed medication in the world. [11-12].

![Figure 1: structural formula of metformin drug](image)

1.1 Physical properties of the drug

- Solid in standard conditions STP
- Melting point m.p5224.5
- Refractivity. 56.642

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1.2 Side effect of metformin

- metallic taste in the mouth
- diarrhea
- nausea of vomiting
- swelling
- Double the appetite
- fast heart rate
- Headache
- It may cause anemia or cause a decrease in the absorption of vitamin B$_{12}$.
- It also causes a condition called Lactic acid [15-17]

1.3 Metformin Bioavailability

Bioavailability of metformin is confined to (50-60%) and is in the main absorbed in the small intestine. The concentration of the drug has been determined in the plasma up to a maximum of two hours after taking the dose by using mouth, and that the drug accumulates in the partitions of the intestine and small salivary glands as properly as in the kidneys. [18-19]

1.4 Metformin use as chelating complex

Metformin possesses two organizations of amines at the site (cis) and thus acts as a clinked, and this makes it an great capability to shape coordination complexes with specific transition metallic ions the place metformin can bind to the transition steel ions either via the 0.33 nitrogen atom (N$_3$) or from By the 2d and fourth nitrogen atoms (N$_2$-N$_4$) [20-23], metformin coordinates with the a number of ions of the transition elements and gives chelating complexes of unique colors, mainly with the following transitional elements] Cu (II), Ni (II), Co (II), Pt (II) [24]. Fig.2 shows the reaction of consistency of metformin with Biting transition metal ions.

1.5 Previous studies to estimate metformin

There are several methods used to estimate metformin in pharmaceutical preparations and in serum samples in addition to multiple environmental models. These spectroscopic, chromatographic and physical methods and table (1) show the estimation of metformin with different techniques.
A simple, fast and accurate method was developed to estimate the spectral metformin hydrochloride and the proposed method is based on the oxidation of 1-naphtholite by sodium hypochlorite and its conjugation with metformin hydrochloride in the presence of sodium hydroxide to form a soluble blue complex, its maximum absorption was (385nm) for the resulting blue complex. The relative standard deviation of the method is better than 1.8%.

Metformin hydrochloride was estimated in some pharmaceutical preparations and in a model of industrial water offered. The method was simple, with high accuracy and high sensitivity. The method was performed by oxidizing metformin with sodium hypochlorite in a basic medium and the maximum absorption was (385nm) for the resulting blue complex. The relative standard deviation of the method is better than 1.8%.

At the same time, both metformin hydrochloride and cliklazide were prescribed in the drugs by using ultraviolet spectroscopy using wavelengths (200-400) nm with a buffer solution of phosphate with a hydrogen concentration (6.8). The method was successfully applied to a pharmaceutical composition. The method was simple, fast and can be used

Developed a spectral method characterized by accuracy, ease and speed to estimate the drug metformin hydrochloride in pharmaceutical preparations and in environmental models where it depends on the interaction of copper with the drug in the presence of a basic medium (ion jackets) where a complex of purple color is formed at a wavelength of 570nm

A selective and sensitive method was developed for determining metformin in plasma and circulation, using a high-performance liquid chromatography by using synthetic membrane selective electrodes where the drug selective electrodes were prepared with the active substance phosphomolytic acid (PHOSPHOMOLYBDIC) or phosphine toxic acid (PHOSPHOTUNGSTIC) and using organic coloring materials butyl phthalates.

A selective and sensitive method was developed for determining metformin in plasma and circulation, using a high-performance liquid chromatography, using a reversible column C18 where the drug was extracted very efficiently by a mixture of butanol and hexane in a ratio of (50:50) v. The moving phase consisted of acetoniitrile and potassium phosphate. Acidity ratio (66:34)

A sensitive and simple method for estimating metformin in human plasma. A number of factors affecting the improvement of the proposed method such as temperature, acidity and reaction time were studied. The process is accomplished by forming a metformin complex with N-methyl bis (trifluoroacetamidet).

A fast and simple method was developed for estimating metformin in the serum by using an infusion injection and using an MS / MS mass spectrometer to analyze the results. Deuterium was used for internal measurement.

| Method          | Comment                                                                 | Linear Range          | Limit of Detection | Ref. |
|-----------------|--------------------------------------------------------------------------|-----------------------|--------------------|------|
| Spectrophotometry | An easy, economical and simple spectroscopic method was used to estimate metformin hydrochloride in large quantities in doses of pharmaceutical preparations using NaOH 0.01N and at a wavelength of 233nm | (1-25) µg.ml⁻¹        | (0.22) µg.ml⁻¹     | [25] |
| Spectrophotometry | A modern spectroscopic method was developed for estimating the drug metformin hydrochloride, as it was used to analyze many commercial pharmaceuticals through the formation of a complex with a bilateral copper ion in a basic medium and measured at a wavelength of 530nm by continuous runoff injection and a linear range of the method was reached at 94.04% | (0.0-100) mM          | 662ng  | [26] |
| Spectrophotometry | A simple, fast and accurate method was developed to estimate the spectral metformin hydrochloride and the proposed method is based on the oxidation of 1-naphtholite by sodium hypochlorite and its conjugation with metformin hydrochloride in the presence of sodium hydroxide to form a soluble blue complex, its maximum absorption (580nm) | (2-20)µg/ml           | (0.7) µg/ml        | [27] |
| Spectrophotometry | Metformin hydrochloride was estimated in some pharmaceutical preparations and in a model of industrial water offered. The method was simple, with high accuracy and high sensitivity. The method was performed by oxidizing metformin with sodium hypochlorite in a basic medium and the maximum absorption was (385nm) for the resulting blue complex. The relative standard deviation of the method is better than 1.8% | 0.5-4 µg/ml           | 0.083 µg/ml        | [28] |
| Spectrophotometry | At the same time, both metformin hydrochloride and cliklazide were prescribed in the drugs by using ultraviolet spectroscopy using wavelengths (200-400) nm with a buffer solution of phosphate with a hydrogen concentration (6.8). The method was successfully applied to a pharmaceutical composition. The method was simple, fast and can be used | (1-20µg/ml)           | 0.0965 µg/ml        | [29] |
| Spectrophotometry | Developed a spectral method characterized by accuracy, ease and speed to estimate the drug metformin hydrochloride in pharmaceutical preparations and in environmental models where it depends on the interaction of copper with the drug in the presence of a basic medium (ion jackets) where a complex of purple color is formed at a wavelength of 570nm | 10- (100µg.ml⁻¹)      | 1.7 µgml            | [30] |
| HPLC            | Quantify metformin hydrochloride in a manner High performance liquid chromatography by using synthetic membrane selective electrodes where the drug selective electrodes were prepared with the active substance phosphomolytic acid (PHOSPHOMOLYBDIC) or phosphine toxic acid (PHOSPHOTUNGSTIC) and using organic coloring materials butyl phthalates. | (10⁻¹-10⁻³M)          | 2.5x10⁻⁷ (M)        | [31] |
| HPLC            | A selective and sensitive method was developed for determining metformin in plasma and circulation, using a high-performance liquid chromatography, using a reversible column C18 where the drug was extracted very efficiently by a mixture of butanol and hexane in a ratio of (50:50) v. The moving phase consisted of acetoniitrile and potassium phosphate. Acidity ratio (66:34) | (10-5000) ng/ml       | 7.8 ng/ml           | [32] |
| HPLC            | This study demonstrates the development of a method for estimating metformin with ACE inhibitors at the same time via HPLC technology. The mobile phase consists of acetoniitrile and water in a 50:50 ratio | 10-10000 ng.ml⁻¹      | 0.98 ng.ml⁻¹        | [33] |
| RP-HPLC         | Determination of metformin with lenacliptin simultaneously. The mobile phase used in this technique consisted of phosphate, methanol, and acetoniitrile at a ratio of 65:10:25. | 125-750 µg.ml⁻¹       | 3.08 µg.ml⁻¹        | [34] |
| GC-MS           | A sensitive and simple method for estimating metformin in human plasma. A number of factors affecting the improvement of the proposed method such as temperature, acidity and reaction time were studied. The process is accomplished by forming a metformin complex with N-methyl bis (trifluoroacetamidet). | 100-3000 ng.ml⁻¹      | 40 ng.ml⁻¹          | [35] |
| Flow Injection MS/MS | A fast and simple method was developed for estimating metformin in the serum by using an infusion injection and using an MS / MS mass spectrometer to analyze the results. Deuterium was used for internal measurement. | 5-2340 ng/ml          | 0.66 ng/ml          | [36] |

Table 1: Estimation of metformin hydrochloride drug with different techniques
Flow Injection

The development of a rapid and sensitive analytical method for estimating metformin by means of a complex formation of a system: metformin-sodium hydroxide - copper ion (II) contained within the gel and using the infusion system. The method was based on a complex composition between the displaced copper ion of the gel and the metformin drug in a basal medium a redish-burgundy color which is absorbed at 530nm.

(0.001-1) mmol.L⁻¹
0.5 μmol.L⁻¹ [37]

Flow Injection

Determination of metformin in pharmaceutical preparations and biological fluids by means of β-cyclo dextrians sensors. The manufactured electrodes contain the sensor ion holder, ionic sites and plastic materials in addition to the coated wire electrodes. One of the advantages of this method is that 90 samples can be analyzed in a simple and sensitive way.

(10⁻¹⁻¹⁰⁶)M
8x10⁵M [38]

Flow Injection

Fluorescence

This method is based on (CL) chemiluminescence of chemical fluorescence by oxidizing N-bromo succinic imide in an alkaline medium with the presence of a fluorescence process and using an acetylcholine such as ammonium bromide.

(7x10⁻², 3x10⁻⁵)
g.ml⁻¹
2.3x10⁻⁹ g.ml⁻¹ [39]

2. Conclusions

In this review different methods for estimation of metformin hydrochloride for pharmaceutical preparation and wide range of the instrumental technique to estimation most of these methods are time consume and complex. All instrumental methods to determination metformin hydrochloride provide the simplicity, sensitivity, low detection limit, accuracy, rapid analysis and economical methods analytical to estimation this drug.

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