

Review on spectroscopic analytical methods for determination of metformin hydrochloride

Nisreen Kais Abood¹, Dalia Mahmood², Amina M.Abass²

¹ Department of Chemistry, College of Science, Mustansiriyah University Baghdad, Iraq

² Department of Chemistry, College of Science, Al-Nahrain University, Al-Jaderia, Baghdad-Iraq

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.

©2020 ijrei.com. All rights reserved

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 $C_4H_{11}N_5.HCL$ [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].

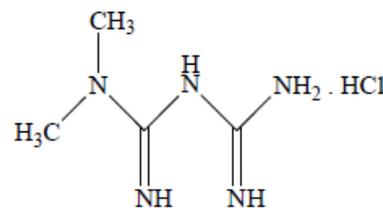


Figure 1: structural formula of metformin drug

1.1 Physical properties of the drug

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

Corresponding author: Amina M. Abass

Email Address: aminamohsen75@gmail.com

<https://doi.org/10.36037/IJREI.2020.4203>

- Polarize ability 13.42
- Molecular Weight (165.6gm / mol). [13-14].

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 B₁₂.
- 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 (N₃) or from By the 2d and fourth nitrogen atoms (N₂-N₄) [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.

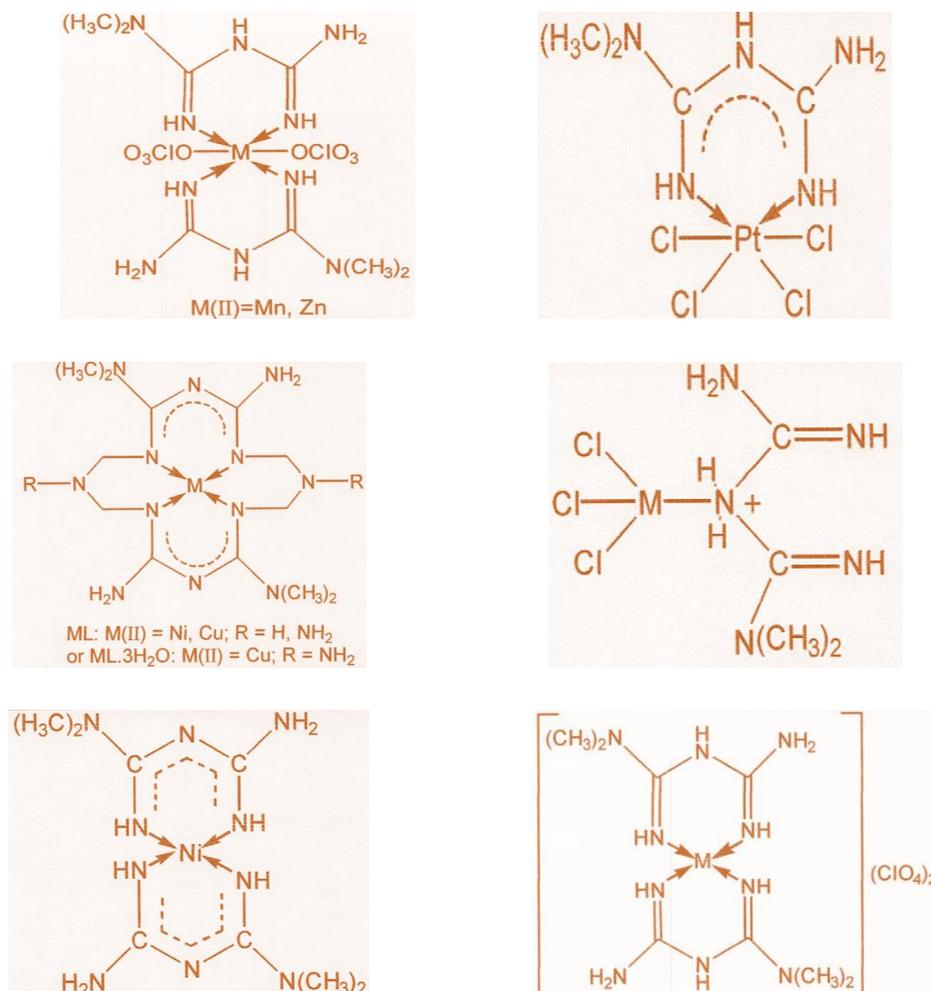


Figure 2: process of symmetry of metformin with some transition metal ions

Table 1: Estimation of metformin hydrochloride drug with different techniques

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) $\mu\text{g.ml}^{-1}$	(0.22) $\mu\text{g.ml}^{-1}$	[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) $\mu\text{g/ml}$	(0.7) $\mu\text{g/ml}$	[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 $\mu\text{g/ml}$	0.083 $\mu\text{g/ml}$	[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	(1-20) $\mu\text{g/ml}$	0.0965 $\mu\text{g/ml}$	[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- (100 $\mu\text{g.ml}^{-1}$)	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 phosphomolybdic acid (PHOSPHOMOLYBDIC) Or phosphine toxic acid (PHOSPHOTUNGSTIC) and using organic coloring materials butyl phthalates.	(10^{-1} - 10^{-5} M)	2.5×10^{-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 acetonitrile 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 acetonitrile 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 acetonitrile at a ratio of 65:10:25.	125-750 $\mu\text{g.ml}^{-1}$	3.08 $\mu\text{g.ml}^{-1}$	[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 (trifluoroacetamide).)	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]

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 reddish-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 dextrins 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	(10 ⁻¹ -10 ⁻⁶)M	8x10 ⁻⁷ M	[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 ⁻⁹ -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.

References

- Wang. Y, Tang. Y, Fawcett. JP, and Bai. X, " Rapid and sensitive liquid chromatography-tandem mass spectrometric method for quantitation of Metformin in human plasma", J chromatography B., 808, 9-215, (2004).
- Lalhriatpuii. T, Kawathekar. N, "Derivative spectrophotometric estimation of pioglitazone and metformin hydrochloride", Indian Drugs. ; 42(11):740-3, (2005).
- R. Nelson , D. Spann, D. Elliott, A. Bronds, and R. Vuliet , "J. of veterinary inter. Med. ,18,8-24, (2004)
- Prachi. S, Ajay. S, R, Nilesh. G, "UV Spectrophotometric method for the quantitation of metformin hydrochloride in pharmaceutical dosage form", Oriental J. Of Chem., 4, 1553-1556, (2010).
- Gusler. G, Gorsline. J, Zhang. S, Berner. B," Pharmacokinetics of metformin gastric-retentive tablets in healthy volunteers", J, of clin. Pharmacology, 41, 655-661, (2001).
- S. Wang, H. Kusuvara, Y. Kato, W. Jonker, and Y, "Involvement of organic cation transporter 1 in the lactic acidosis caused by metformin ", Molecular pharmacology, 16(4), 8-844, (2003).
- Dorman. T, "Double-blind evaluation of efficacy and tolerability to metformin in NIDDM ", Diabetes care, 14, 342-344, (1991).
- Stepensky. D, Friedman. M, Srour. W, Raz. I, Hoffman. A, "Preclinical evaluation of pharmacokinetic-pharmacodynamic rationale for oral CR metformin formulation", J. control Release , 71, 107-117, (2001).
- Arayne MS, Sultana N, Zuberi. MH and Siddiqui. FA, "Spectrophotometric quantitation of Metformin in bulk drug and pharmaceutical formulation using multivariate technique"; india J. pharma, 71,331-335, (2009).
- Agarawal. Y. K, Gogoi. P. J, Manna. K, Bhatt. H. G, "Supercritical fluid Chromatography tandem mass spectrometry method for the simultaneous quantification of metformin and glicaside in human plasma", Indian j. pharma, 72, 7-50, (2010).
- Bailey. CJ, Day. C, "Metformin its botanical Background", John wiley&Sons, Ltd, 115-117, (2009).
- The use of Medicines in the United States: Review of 2010, institute for health care informatics, (2011).
- Vogel's Text book of Quantitative chemical Analysis, 6th Ed PearsEdu Ltd, Singapor, (1989).
- The council of the Royal pharmaceutical society of Great Britain, The Extra pharmacopoeia, published by Royal pharmaceutical society, UK, 357, (2005).
- Bodmer. M, Meier. C, Jick. SS, " Metformin sulfonylureas or other antidiabetes drugs and the risk of lactic acidosis or hypoglycemia: a nested case-control analysis"; Diabetes care, 31, 2086-2091, (2008).
- Rossing. P, Rossing. K, Gaede. P, Pederson. O, Parving. HH, "Monitoring Kidney function in type 2 diabetic patients with incipient and overt diabetic nephropathy", Diabetes care, 29, 1024-1030, (2006).
- Jolien. D. J, Andrian. K, Ab. M. J. Donker, Michiel. G. W, "Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: Randomised placebo controlled trial", BMJ (2010).
- Wilcock. C, Bailey. CJ, "Accumulation of metformin by tissues of the normal and diabetic mouse", Xenobiotica; 24: 49-57, (1994).
- Scheen. AJ, "Clinical pharmacokinetics of metformin", Clin Pharmacokinet, 30: 359-371, (1996).
- Bentefrilt. F, Morgent. G, Viossat. B, Leonce. S, J. Inorg. Biochem 68, p: 53-59, (1997).
- Gowdhury. S. R, Sipani. M. K, J. Indian chem., 65, 718, (1988).
- Miaoli. Z, Liping. L, Pin. Y, Xianglin. J, "Bis (1,1-dimethyl biguanido) nickel(II)"; Acta Cry. , 58, p: 272, (2002).
- Olar. R, Badea. M, Marineescu. D, Chifiriue. M, "displaying low cytotoxicity as potential large spectrum antimicrobial agents"; N, N-dimethyl biguanide complexes displaying low cytotoxicity as potential large spectrum antimicrobial agents", Eur. J. Med. Chem., 45, 3027-3034, (2010).
- Tomas. A, Viossat. B, Dung. N. H," L' hydrogenocarbonate de Bis(N,N-dimethyl biguanide) Cuivre(II) ", Acta. Cryst, 51, 213-215, (1995).
- Reatul. K, Nurunnahar. P, Rebecca. B, "Development and validation of UV spectroscopic method for the determination of metformin hydrochloride in tablet dosage form", International J. Ph. Sci. and Res., 3(9), 3170-3174, (2012).
- Issam. M. A, Basim. I, Huda. M. N, "Continuous Flow injection Analysis (CFIA) of Metformin Hydrochloride using Microphotometer Equipped with 530 and 550nm LED", J. of Al-Nahrain Uni. , 16(4), 29-36, (2013).
- Nief. R. A, Farah. K. O, "Spectrophotometric determination of metformin hydrochloride via oxidative coupling reaction with 1-naphthol in pharmaceutical and environmental water sample", Iraq National J. of chem. ; 46, 161-170, (2012).
- Nief. R. A, "Facial visible spectrophotometric determination of metformin hydrochloride in glucosam and industrial waste: Application to content uniformity testing", Iraq pharma; 12, No.1, (2012).
- Radhika. B, Rahul. B, Mahendra. K. S, Vipin, "Uv-Spectrophotometric-Assisted of metformin hydrochloride and Gliclazide in pharmaceutical formulations"; ph. Anal. Acta, 2153-2435, (2012).
- Nief. R. A, "Spectrophotometric determination of metformin in pharmaceutical preparation (tablets) and environmental water samples: Application to content uniformity testing"; Iraq National J. of chem., 47, 300-310, (2012).
- Ali I. Khaleel ,Suham T. Amine and Emad M. Yousif" Determination of Metformine Hydrochloride Drug by Using of Manufactured Selective Membrane Electrodes and High Performance Liquid Chromatography Method HPLC" Raf. J. Sci., Vol. 21, No.3, pp. 138-157, (2010).
- Raniah Q.G, and Raj S.P., "Determination of Metformin in Human Plasma and Urine by High - Performance Liquid Chromatography Using Small Sample Volume and Conventional Octadecyl Silane Column", J. Ph. Pharmaceut, 13(4), 486-494, (2010).

- [33] Farhan. A. S, Nawab. S, Saima. S. B, Concurrent determination of metformin and some ACE inhibitors: its application to pharmacokinetics, 2013
- [34] Sheena. M, Rohini. R, "Simultaneous determination of metformin hydrochloride and linagliptin by RP-HPLC in bulk and pharmaceutical formulation", Indo Amer. J. of pharm. Reas., 4, 4047-4053, (2014).
- [35] Ebru. U, "The development and validation of gas chromatography-mass spectrometry method for the determination of metformin in human plasma" Royal soci. Chem., 5, 4723-4730, (2013).
- [36] Deborah. M, Terra. A, Anas . EL, "Development and validation of fast and simple Flow injection Analysis- tandem mass spectrometry (FIA-MS/MS) for the determination of metformin in dog serum ", J. of ph. and Biom. Anal. ; 107, 229-235, (2015).
- [37] Issam. M. A, Nagam. S. T, "Continuous Flow Injaction Analysis for the photometric determination of metformin drug via the realese of copper (II) ion from charged Gel bead crystal", Iraq J. of sci., 54, 17-26, (2013).
- [38] Khaled. E, Kamel. MS, Hassan. HN, Abd El-Alim. SH. Enein. HY, Miniaturized ionophore-based potentiometric sensors for the flow-injection determination for metformin in pharmaceutical formulations and biological fluids", National institutes of health, 137(23), 7-5680, (2012).
- [39] Zhouping. W, Zhujum. Z, Zhifeng. Fu, Wanfem. L, Xiao. Z, "Sensitive Flow-injection chemiluminescence determination of metformin based on N-Bromosuccinimide-fluorescein system", J. Anal. Letters-Anal let, 36, 2683-2697, (2003).

Cite this article as: Nisreen Kais Abood, Dalia Mahmood, Amina M.Abass, Review on spectroscopic analytical methods for determination of metformin hydrochloride, International Journal of Research in Engineering and Innovation Vol-4, Issue-2 (2020), 91-95. <https://doi.org/10.36037/IJREI.2020.4203>.