Nano Synthesis and Characterization of Complex Derived from Silver Metal Conjugated with Midodrine Hydrochloride

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http://dx.doi.org/10.13005/ojc/370121

(Received: January 22, 2021; Accepted: February 22, 2021)

ABSTRACT

The stability constant $K_f$ for the complexation of Ag(I) metal ion with Midodrine hydrochloride were determined by spectrophotometric method at room temperature. The colored complexes were measured at 300 nm. The stability constant of the complexes were found to be 5.47 by mole ratio method. The stoichiometry of the complexes formed between the Midodrine drug and Ag(I) metal ion are 1:1 M/L ratio. Silver conjugated Midodrine hydrochloride Nano synthesized and characterized by UV-Visible spectroscopy, SEM, XRD and FT-IR. The UV-Visible spectra of Midodrine-Ag nanoparticle in the range of 322 nm. XRD conform The crystallite size of Midodrine-Ag nanoparticles are found to be 64.5 nm from Debye Scherer formula. The crystallinity of nanoparticles is Face centered cubic structure. SEM conform of particle size and surface morphology, FTIR analyzed involvement of $-\text{NH}_2$ group in Midodrine is the stabilized of silver nanoparticle. This research is focuses on complexation, Nano synthesis and characterization of Drug-silver nanoparticle for antihypotention therapy.

Keywords: Complexation, Antihypotensive drug, Nano synthesis, XRD, SEM, FT-IR.

INTRODUCTION

One of the antihypotensive drugs, midodrine hydrochloride chemical name 2-amino-$N$-[2-$(2$, 5-dimethoxyphenyl) hydroxyethyl] acetamide; hydrochloride and chemical formula is $\text{C}_{12}\text{H}_{19}\text{ClN}_{2}\text{O}_{4}$ which is used for the treatment of low blood pressure that upgrade the blood pressure. That drug involves the shrinking of blood vessels and elevated blood pressure$^2$. The interaction of antihypotensive drug Midodrine with Ag(I) ion lead to formation of complexes. Nanotechnology representation, one of the great breaks through of warrant matter which is formed thought the different composition of material size and structure. Nano material is distributed based on their size 1-100 nm. That nanoparticle or nanomaterial are seen decomposition or reduced at atomic and polymer material and they show different chemical, physical and spectral properties. Preparations of nanoparticle are need to their utilization and this remains a field of active research$^3$ where drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix.

Nano capsules are system in which were Midodrine is cramped to a cavity of silver metal ion and that metal ion is surrounded by ligand Midodrine$^4$. Inorganic nanomaterials have attracted...
much attention as drug carriers due to their excellent biocompatibility, bioactivity, and lack of susceptibility towards immune system\(^5\).

Nanoparticle-based drug delivery systems have been developed and that show several advantages like improved solubility of drug in serum, increased half-life of drug in body, controlled and targeted drug release, currently these systems have now been employed for combination therapy using multiple drugs targeting identical cells\(^6\). In field of Nano medicines there are many merits, the magnification of drug absorption into tissues, refinement of their mode of action, and developments of intracellular tissues\(^7\)\(^8\). Due to their different physicochemical property like optical, electronic and magnetic property drug –Ag Nps has been studied extensively\(^9\).

**MATERIALS AND METHODOLOGY**

**Instrumentation**-Systronic UV-Visible double beam spectrophotometer type 118 and 1cm quartz cell were used for the absorption spectra. Sartorius BSA224S–CW electronic chemical balances are used for accurately weight of chemical. Systronic pH system 361 is a high performance pH meter is used for adjusting pH of buffer solution and complexes.

**Reagents**

All chemical were used of analytical grade. Drug Midodrine hydrochloride purchased from TCI chemical Pvt Ltd (India). Analytical grade nitrate salt of silver and phosphate buffer purchased from Merck. Sodium borohydride and sodium citrate from merck. For all working solution deionized water is used.

**Preparation of standard Stock solution**

Midodrine hydrochloride (1×10\(^{-2}\) M) is prepared by 1.27 g dissolved in deionized water and makeup up to 100 ml volumetric flask\(^10\). Metal stock solution is prepared by dissolving Silver nitrate (M.W.– 169.8, 0.1 M 0.849 g) dissolved in deionized water and then makeup to the mark in 100 mL volumetric flask. Sodium borohydride 5mM, M.W. 37.83 is freshly prepared by dissolving 0.189 g in deionized water and make up into 100 ml volumetric flask.

**Complexation of midodrine hydrochloride with Ag (I) metal ion**

A series of solution mixtures are prepared with a variable concentration of Midodrine and constant Ag (I) Metal ion in mL. Midodrine solution varying from 0.5 mL - 3.5 mL and 1.0 mL of silver nitrate solution added each solution of midodrine. Added 4 mL of buffer solution and makeup up to 10 mL measuring flask with deionized water. Mixtures are allowed to stand 20 minute. Blank solution is prepared by midodrine drug and deionized water. The higher absorbance of blank solution is standard value of wavelength. And this wavelength are selected for analysis the absorbance of series solution. The absorption spectra of these mixtures were recorded at 35°C. The analysis is reported in tabulated and graphical form.

**Determination of Stability Constant by mole ratio method**–

Stoichiometric of complexes formed in the solution determined by spectrophotometric applying mole ratio method\(^12\). The logarithmic constant \(\log K_f\) and the free energy change \(\Delta G\) of form complexes are calculated from the data of mole ratio method applying equation 1 & 2. The equation for mole ratio method is

\[
K_f = \frac{A/e_b}{[CM - A/e_b] \times [CL - A/e_b]} 
\]

\[
\Delta G = -2.303 RT \log K_f 
\]

Where \(e_b\) = molar absorptivity, \(A\) = absorbance at peak point, \(CM\) = concentration of metal, \(C_L\) = concentration of ligand, \(T\) is the absolute temperature and \(R\) is the gas Constant.

**Synthesis of Midodrine conjugated Ag Nps**

Midodrine -Ag Nps are synthesized. 10 mL (1×10\(^{-2}\) M) of Midodrine solution added in 10 mL (1×10\(^{-1}\) M) AgNO\(_3\). This solution mixture is magnetically stirred for 15 minute. After that NaBH\(_4\) which is freshly prepared added 25 ml (5×10\(^{-3}\) M) drop wise in the reaction mixture. Suddenly reaction mixture solution colour turned transparent to dirty Brown, Centrifuged Nanoparticle at 5,000 × g for 8 h supernatant particles was dried at 50°C and collected the nanoparticle sample.

**Characterization of Drug –Ag conjugated Nps**

The prepared nano conjugated midodrine-
Ag(I) NPs characterized by several analytical techniques and the obtained data is analyzed. Visible spectroscopy gives the absorption and optical properties of the prepared nanoparticle. X-ray diffraction patterns give the crystalline structure, SEM was used to monitor the size and shape FT-IR reveals the presence of functional group bond and other bonds in the sample. The results obtained from the above investigations are analyzed for confirming the nanoparticle of drug conjugated Ag(I) nanoparticles.

**RESULT AND DISCUSSION**

**Table 1: Spectrophotometric experimental data for complexation of midodrine –Ag(I) by mole ratio method**

| Metal ion concentration | Ligand concentration | O.D at 300 nm |
|-------------------------|----------------------|--------------|
| 1×10^{-1} mol (mL)      | 1×10^{-2} mol (mL)   |              |
| 0.5                     | 1                    | 2.826        |
| 1                       | 1                    | 3.014        |
| 1.5                     | 1                    | 2.928        |
| 2                       | 1                    | 2.883        |
| 2.5                     | 1                    | 2.97         |
| 3                       | 1                    | 2.983        |
| 3.5                     | 1                    | 2.99         |

**UV-Visible spectroscopy**

The nanoparticle formation can easily be monitored through its distinctive color change. Within the first minute of sodium borohydride injected with drug -Ag(I) complex. The solution became light brown. Addition of NaBH₄ is indicate reduction of Ag(I) metal ion and the formation of Midodrine –Ag NPs. Drug–Ag(I) NPs are preparatory characterized by using UV-Visible double beam spectrophotometer.

UV-Spectrophotometric analysis of Drug–Ag(I) complex are monitored from 200 nm to 800 nm, and a strong peak specific to synthesized nanoparticle are observed at 322 nm. The ratio of optimization rated to be 1:1 for midodrine and Ag(I) metal ion. The optimizing ratio at which maximum absorbance of UV-Vis spectrum found, considered as Midodrine-Ag(I) nanoparticles are synthesized. UV-Vis spectra of Midodrine conjugated Ag(I) nanoparticles appear a sharp peak at 322 nm.

**X-ray diffraction (XRD) analysis**

X-ray diffraction is the most important techniques to acknowledge analyzed structural properties of synthesized NPs. It gives adequate information about the crystallinity and plane of NPs. That techniques functioning well for both single and multiphase nanoparticle identification. The X-ray diffraction (XRD) patterns of prepared Midodrine conjugated Ag(I) nanoparticles identified by using X-ray diffractometer along CuKα radiation (λ = 1.5406 Å) is shown in Figure 3.
The intense peaks at 2θ values of Midodrine-Ag(I) 38.200, 44.43°, 64.45°, 77.63 0, 81.670, Corresponds to the planes of (111), (200), (220), (311), (222). 32.37, 46.38 respectively. In addition to these peaks, possibly due to organic compound crystal present in the sample conforms the Ag(I) nanoparticles matching with JCPDS Card No. 04-0783. The crystalline size of midodrine-Ag(I) nanoparticles was found to be 64.5 nm & from Debye Scherer formula. It is observed that the crystal structure of silver nanoparticles is FCC (Face centered cubic) based on the above planes (111), (200), (220), (311), (222). The diffractogram pattern conforms highly crystalline nature of synthesized materials as Midodrine-Ag (I) nanoparticles.

**Scanning Electron Microscopy (SEM)**

Scanning electron microscopy is used for the analysis of particle shape and morphology of microelement/trace element nanoparticles and also conjugated nanomaterial. For analysis of SEM, fine powder of Midodrine –Ag NPs are used. SEM images of conjugated Drug-Ag nanoparticles are recorded by JSM-6510LV scanning electron microscope (JEOL, Tokyo, Japan) operated at speed up voltage of 30 kV. For SEM image, a pinch of synthesized Midodrine-Ag(I) nanoparticles are placed on carbon coated grid at potential set off 110 KeV. Average particles size of drug conjugated Ag (I) nanoparticles is 64 nm.

Figure 4 represents the SEM micrographs of Midodrine -Ag(I) Nanoparticles observed at different magnifications. The SEM images represent the agglomeration of particles. It is also be seen that the samples synthesized were Nano flakes which were turned to the particles when observed at different magnification.

**FTIR Analysis**

FTIR technique is helpful for the identification of ligand functionalities which is responsible for stability of nanoparticle. It is well reported that drug functional group were involve in capping agent the synthesis drug conjugated with Ag Nanoparticle and it is analyzed by FTIR with the help of this enable to recognize which functional group involved in Midodrine-Ag Nps nano-synthesis.

The FTIR spectrum of midodrine hydrochloride/Ag nano particle revealed the present of absorption peak at 3741 cm\(^{-1}\) 2887 cm\(^{-1}\) for C-H stretching frequency furthermore the presence of 1630 cm\(^{-1}\) and 1530 cm\(^{-1}\) peaks was associated for C=C and amide bonding of organic ligand and the slightly broad peak of 1317 cm\(^{-1}\) –N-C stretching of ligand and 1150 cm\(^{-1}\) C-O stretching 662 cm\(^{-1}\) is for carbon halogen bond group (Fig. 5) and the high intensity peak of 1000 cm\(^{-1}\) is significant peak of Ag. From the IR data all functionalities of Midodrine were involved and intense peak of Ag conform the Nano synthesis of our complex. Mido-Ag Nps. prefers to bind primary NH\(_2\) group. We can conclude that the organic ligand is successfully binded with Ag metal ion.

**CONCLUSION**

The complexation of drug Midodrine hydrochloride and metal ion developed a new metal based drug, which could act against human hypotension. The work is successfully demonstrated that the use of UV-Visible spectroscopy is feasible
in complexation reaction and stability constant. It was found that Drug and metal forms stable 1:1 (M/L) ratio of complexes. In new drug, based metal ion complexes, silver nanoparticle have many properties which demonstrate their potential use in hypotension therapy and that is easily synthesized by using chemical reduction agent such as sodium borohydride using standard procedure.

This complex is successfully Nano synthesized, characterized and conformed by UV-Visible spectroscopy, XRD, SEM, FTIR. Silver Nano synthesized drug represent a research field of increasing progress of pharmaceutical profile like biological activity of drugs, development of modified drugs, Decreases dosage of drugs. Anthypotensive drug as a chelating agents can be used for analysis of trace element ion.

ACKNOWLEDGEMENT

The authors are grateful to Dr. C.V. Raman for their valuable support. The authors also like to give special thanks to metallurgy department of NIT Raipur and Pt. Ravi Shankar Shukla University Raipur for assistance in instruments analysis.

Conflicts of interest

Authors declare that they have no conflicts of interest.

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