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Electrochemical behavior of Metronidazole (MNZ) at glassy carbon electrode at different concentrations

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Abstract: A robust and straightforward electrochemical methodology based on electrochemical detection of Metronidazole (MNZ) at glassy carbon electrodes was suggested to determine. MNZ formed well-defined reversible cyclic voltammograms on the glassy carbon electrode in the Britton Robinson buffer solution. Various parameters' effects on voltammetric results were also evaluated. For MNZ determination, a differential pulse voltammetric model was introduced and developed. Excellent recovery results for spiked MNZ in pharmaceutical tablet samples were obtained, with recovery rates ranging from 97.44 to 97.51 percent.

Keywords: Electrochemical method; Metronidazole; Britton Robinson buffer solution.

1. Introduction

Metronidazole (MNZ) is a synthetic imidazole analog extensively used in the oral treatment of Entamoeba histolytica, Giardia lamblia, Gardnerella vaginalis, and Trichomonas vaginalis infections. Therefore, determining and controlling the MNZ component in food and pharmaceuticals is critical for human health and food safety.

Antibiotics are a class of drugs used to treat diseases in people and animals. Antibiotic use has increased in the past few years, increasing the prevalence of pharmaceutical compounds in the environment via wastewater, particularly in aquatic habitats. This circumstance represents a severe threat to the health of all living beings.

Risks of teratogenicity, carcinogenicity, and nerve mutagenesis have all been utilized by Metronidazole. As a result, high accuracy and specific quantitative detection of Metronidazole are essential, and its regulation in food and medicines is a serious issue regarding human health and food safety [1].

MNZ has been used to treat infectious infections for over 50 years effectively. MNZ showed substantial activity against gram-negative and gram-positive anaerobic bacteria, such as Bacteroides fragilis and Clostridium difficile [2].

Developing appropriate drug carrier systems in nanostructured form is one of the unique ways to overcome this difficulty. Using Nanocarriers offers various advantages, including enhancing the medication's solubility and bioavailability, prolonging the drug's time in circulation and controlling its release, and lowering the required dose and side effects while delaying bacterial resistance as far as possible [2].

MNZ, a synthesized pharmaceutical drug used to treat trichomoniasis, diarrhea, liver abscess, skin disease, aerobically infected burn sites, and surgical prophylaxis, was selected to check the electrochemical sensors. Sepsis is a leading cause of death in patients with burn wounds, owing to the difficulty of maintaining a disinfected environment in the health center and avoiding impurities with bacteria and the subsequent antibiotic hostility [3]. MNZ detection is also vital for reducing side effects such as nausea, diarrhea, neurotoxicity, visual nerve pain, peripheral nerve pain, and narcolepsy. It has also been demonstrated to have Genotoxicity in animal models [3].

The pharmacokinetic profile of traditional MNZ tablets shows that the MNZ is absorbed entirely and quickly after oral administration. The dose type delivers a minimum amount of MNZ for local action in the colon and has undesirable systemic effects, leading to amoebiasis alleviation [4].

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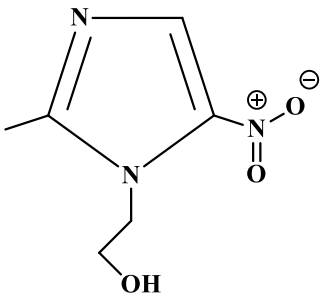
MNZ also treats periodontal disorders, infections, and inflammatory illnesses affecting teeth-supporting tissues, such as gingivitis and periodontitis. When germs from dental plaque infect adjacent tissues, and plaque builds up near the gingival border, an inflammatory response occurs.

Modern medicine faces difficulty combating the increasing problem of antibiotic and chemotherapeutic immunity. Despite enhanced treatment procedures, higher levels of preventive medicine, and increased acknowledgment of drug addiction, the casualty caused by antibiotic-resistant bacterium strains rises yearly. As a result, new molecules with antibacterial potential are being developed, and interest in using noble metals in medicine as an alternative to antibiotics is resurfacing [5].

Because of its limited absorption, a high dose must be given often to achieve a compelling plasma concentration profile for therapy [6].



The molecular structure of metronidazole (**MNZ**).

Electrochemical behavior of Metronidazole

Many electrochemical sensing systems have been developed to detect Metronidazole (MNZ). E.g., Ensafi et al. have done the electrochemical detection of MNZ by a sensing system of graphene nanosheet loaded with graphene quantum dot modified by a molecularly imprinted polymer.

Li et al. also showed an electrochemical detecting method for identifying MNZ using a molecularly imprinted polymer-modified nanoporous nickel framework. Chen et al. reported a core-shell molecularly imprinted modified by polymer sensing method for electrochemical detection of MNZ. In all these studies, the specific surface area was increased by changing the nanomaterial on the electrode. However, the performance of an electrochemical sensor depends not only on the number of recognition sites but also on the conductivity of the modifier material. It is, therefore, imperative to design a sensor capable of analyzing MNZ in various samples [12].

MNZ is a nitroimidazole drug used to treat human parasitic infections, including Giardia-related disorders, amoebic liver abscesses, and Gardnerella vaginitis [13,14].

Since it is a biologically important molecule, electrochemical detection becomes more critical.

Various chemically modified electrodes have been designed for the electrochemical detection of medicine like MNZ, but their presentation of electrochemical performance is not good enough; thus, the evolution of electrodes with superior performance is needed [15].

We eventually used the valued material for the potent electrochemical sensing of MNZ.

Villian ATE et al. Reported a CNF–NiCo-LDH-GCE modified electrode that exhibited outstanding electrocatalytic performance toward detecting MNZ. The fabricated electrode showed high sensitivity and copiability with acceptable reproducibility. A low detection limit and exceptional anti-interference performance for the electrochemical sensing of MNZ and the designed detector can be successfully used to determine MNZ in human plasma, tears, commercial tablets, and human urine at a very-trace level. The synthesized CNF–NiCo-LDH-GCE detectors can be well-founded in real-time and practical demand [16].

Removal efficiency, COD removal rate, and TOC removal rate are For MNZ are 100%, 93.3%, and 79.30%, respectively, when TiONis used as an electrode. Thus this TiON shows high electrocatalytic activity, and it is a promising electrode for effective electrochemical degradation of an antibiotic such as MNZ [17].

Lu S et al. The electrochemical determination of Metronidazole was described by Utilizing the distinctive properties of multi-walled carbon nanotubes, such as high specific surface dimension, good electronic possession, and high adsorptive ability [18].

Ensafi AA et al. Reported A green, simplistic, and cost-effective scheme to synthesize an MNZ sensor based on the cysteic acid/PDDA-GN composite film. The cysteic acid/PDDA-GN composite exhibited excellent electrocatalytic activity to reduce Metronidazole due to the synergistic effect of PDDA-GN and cysteic acid. Furthermore, the broad linear range, low detection limit, and better selectivity of the as-prepared sensor hold potential for the experimental determination of MNZ. Therefore, the high electrochemical presentation and the biocompatibility of the cysteic acid/PDDA-GN composite make it a promising material for electrochemical sensors and further biosensor applications [19].

Ensafi AA et al. Reported a sensor-based technique to determine MNZ, a novel electrochemical sensor GQDs-MIPs/GNPs/GCE was synthesized. This sensor contained high sensitivity and excellent selectivity. This fabricated sensor shows the broad linear range and the low detection limit for MNZ detection. The prepared sensor was successfully used for fast and sensitive

detection of MNZ in actual samples. In addition, the characteristics of the ready detector are compared to another electrochemical sensor for MNZ detection [20].

Salimi A et al. reported the electrochemical reduction of ranitidine and MNZ on a glassy carbon electrode modified with single-walled carbon nanotubes. This approach eliminates the need for chromatographic separation procedures. The ability of the modified electrode to separate the voltammetric response of selected compounds was evaluated. Finally, this modified electrode was used to analyze MNZ in medicinal samples. The results indicate that the modified electrode facilitates the determination of ranitidine and MNZ with Better sensitivity and duplicability than similar-based electrodes [21].

A successful and dependable analytical approach for analyzing medicines in different media is essential. In correlation with other detection mechanisms, the electroanalytical method has many advantages, such as speed, accuracy, and ease of use. In addition, electrochemical methods can also expose the reaction mechanisms of drugs on the working electrode, which allows perceiving their redox processes in vivo. Yuan S et al. Reported electrochemical sensors for detecting MNZ. However, developing and fabricating novel and efficient electrocatalysts as working electrode materials for electrochemical sensing MNZ still faces tremendous difficulties [22].

Zheng B reported a smooth strategy to synthesize an MNZ biosensor based on the PDDA-GN/DNA composite film. This biosensor enhanced electrocatalytic activity in reducing MNZ compared with the bare Glassy carbon electrode due to the synergistic effect of the PDDA-GN and the DNA composite film. The biosensor Demonstrates exceptional signal amplification performance, a broad linear range, a low detection limit, better selectivity, and outstanding repeatability. Furthermore, the biosensor could be implemented to detect MNZ in actual samples with satisfactory results, and it has excellent potential for electrocatalytic and biosensing applications [23].

Baikeli Y reported an iron-doped metal-organic framework Fe/ZIF-8 at an Ambient temperature. Eventually, an iron, Nitrogen co-doped nonporous carbon component Fe/NC was prepared by straight carbonization of Fe/ZIF-8 at 900°C. The Fe/NC composite was used to prepare a chemically modified electrode for the rapid and significantly sensitized detection of MNZ in PBS buffer by CV and LSV. Due to iron atoms' catalytic consequence, rich nitrogen content, large surface area, and distinctive porous structure of the nonporous Fe/NC material, the GC electrodes modified with Fe/NC demonstrated excellent electrochemical performance for MNZ. Maximization of the trial environment and analysis of the samples was carried out in this work. The recovery values of the test data verified that the Fe/ NC component was an excellent electrode modifier for determining these analytes, such as MNZ, in sample [24,25].

MNZ in Ophthalmology

The 5-nitroimidazole derivative MNZ has been established as the medicine of choice to treat numerous systemic protozoal disorders, including amoebiasis and anaerobic bacterial infections.

MNZ's mode of action is based on creating chemicals that damage microbial DNA inside cells. By directly regulating T lymphocytes and causing changes in the activity of neutrophil cells, the medication also has an anti-inflammatory and immunomodulatory impact, reducing the formation of reactive oxygen species.

In addition, Metronidazole is metabolized in vivo into at least five metabolites having biological activity [5].

Antibacterial tests

The lowest concentration inhibiting bacterial growth was used to detect the minimum inhibitory concentration (MIC) of the samples produced. Dilution and culture were performed on 96-well microtiter plates. Overwater dispersion, the greatest applied concentration was 10% (w/v) [4].

In-vitro drug release study

The release of MNZ from salted and unsalted chitosan nanoparticles was studied in vitro. First, 5 ml of 0.15 M PBS solution was used to disperse dry nanoparticles containing 10 mg of MNZ [2].

Bacterial culture in this study

Metronidazole-loaded chitosan nanoparticles were compared to free Metronidazole in their ability to kill Bacteroides fragilis ATCC 23,745 as gram-negative anaerobic bacteria [2].

Drug side effects

Orally administered antimicrobials have a systemic impact; however, this application has some side effects, such as hypersensitivity, gastrointestinal intolerance, and bacterial development [4].

Dizziness, anorexia, seizures, palpitations, skin allergies, digestive issues, joint discomfort, and shortness of breath are among the side effects of MNZ [2]. In addition, in recent years, it has been observed that bacterial resistance to Metronidazole has increased, reducing its vulnerability to Bacteroides species [2].

Drug interactions

Generally, MNZ does not show any interaction with other drugs. Still, when it comes in contact with ethanol, it may provoke a disulfiram-like reaction [7,8]. It could be considered that food intake did not significantly change the bioavailability of Metronidazole. This drug can safely be taken with and between meals. Food intake has little effect on bioavailability, though absorption can be delayed [9]. Anticoagulants (e.g., warfarin), astemizole, busulfan, cisapride, cyclosporine, fluorouracil, LI, macrolide immunosuppressants (e.g., tacrolimus), sulfonylureas (e.g., glipizide), or terfenadine since their behavior and risks of adverse effects can be enhanced.

Side effects

Nausea, constipation, anorexia, epigastric pain, and stomach cramps are the most prevalent side effects. In addition, oral thrush, itchiness, redness, dry mouth, dry vulva and crotch, pelvic discomfort, vertigo, headaches, ataxia, insomnia, and color change of urine can all occur [9,10]. The gastrointestinal tract and nervous system are particularly vulnerable to these side effects, especially at high doses [11]. MNZ should not be taken with azole antifungals (e.g., ketoconazole) or cimetidine, as they may increase the possibility of side effects.

Optimization of DPV parameter for MNZ determination

The influence of differential pulse frequency and scanning speed on the peak current of different concentrations of Metronidazole (MNZ) in pH 5 Britton–Robinson buffer solutions were analyzed collectively at the scale of 100mV and mV/s.

Working electrode GC was modified with the drug alcoholic solution of the drug and cast on a glassy carbon electrode by the droop cast method. Before using it, this electrode was dried at room temperature and was sonicated for 10 to 20 min.

Pt wire was used as the reference electrode and AG

Graph discussion

Cyclic volumetric analysis:- On the scale of -1 to 1.5 A, at different concentration values, MNZ was investigated. Comparing these results, the voltammograms improved significantly when glassy carbon electrodes modified with MNZ were used. The potential was examined at the scan rate of 100 mVs^{-1} for both peak reduction current and peak current (Figure 1 and Table 1).

Pt wire was used as the counter electrode, and Ag/AgCl electrode was used as the reference electrode in this analysis.

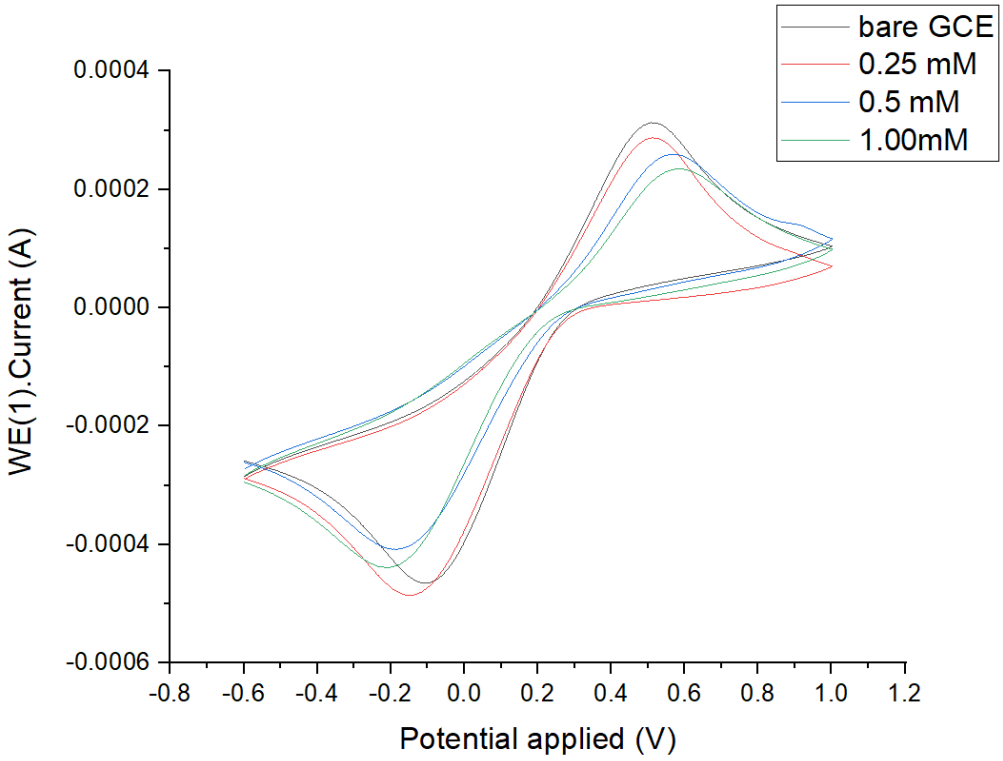


Figure 1. 0.5 mM MNZ cyclic voltammograms in Britton–Robinson buffer solution at various concentrations ((a)–(d): bare GCE, 0.25 mM, 0.5 mM, 1.0 mM respectively) 100 mV s^{-1} scan rate

Table 1. Values of cathodic peak current and anodic peak current & cathodic peak potential and anodic peak potential.

SN	Conc.	E_{Pa}(V)	I_{Pa}(A)	E_{Pc} (v)	I_{Pc}(A)
1	Bare GCE	0.4986	0.0003113	-0.05798	-0.00045
2	0.25Mm	0.527	0.00025174	-0.116	-0.00047
3	0.5Mm	0.508	0.000242	-0.14	-0.0004
4	1.0mM	0.5377	0.000226	-0.15	-0.00042

DPV curve Analysis: Differential pulse voltammograms show distinct peaks for bare GCE and GCE modified with MNZ with different concentrations. These peaks have shown in Table 2 and Figure 2.

Table 2.

SN	Concentration	Potential applied (V)	Current (A)
1	Bare GCE	-0.0569	0.0008773
2	0.25 mM	0.2149	0.000863
3	0.5 mM	0.0740051	0.000384155
4	1.00mM	0.376129	0.000295

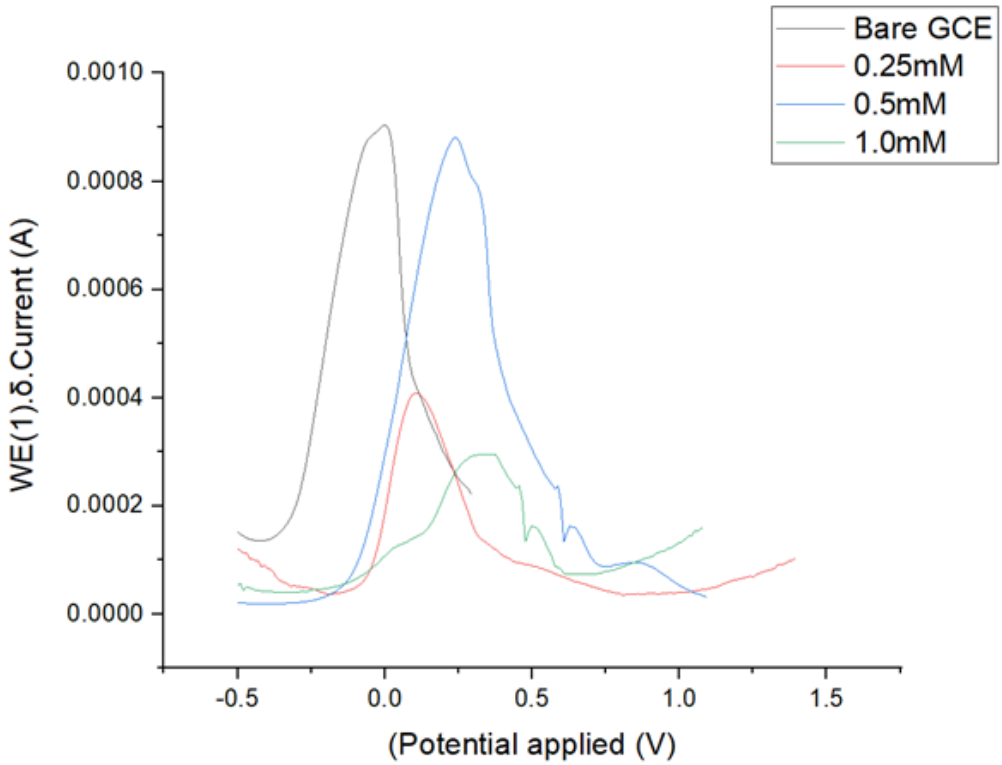


Figure 2. Differential pulse voltammograms in pH 5.0 Britton–Robinson buffer solution with (a) no MNZ (at bare GCE) And Different concentrations of MNZ (0.25mM,0.5mM, and 1.00 mM, respectively)

Drug Delivery Systems

Most drugs were delivered to the colon by colon-targeted delivery systems, recognized and registered. Numerous primary techniques for colon-focused distribution, including prodrugs, pH-dependent processes, and other methods, have seen mixed results. The theory of medicines is used in the osmotic drug delivery system (ODDS). To a large degree, drug release from these processes is independent of pH and other physiological parameters, and there is a strong in vitro–in vivo link. ODDS drug distribution follows a

zero-order kinetic, allowing for greater regulation of in-vivo efficiency. Several forms of osmotic pumps have been identified to target the opioid to the colon for local or systemic treatment. There were systems, after all. However, because of the wide range of gastric retention times, these devices cannot predict the exact location of drug release.

Conclusion

The electroanalytical evaluation of MNZ. Prescription pills and human urine were efficiently carried out using a glassy carbon electrode. The suggested methodology for determining MNZ in specific pharmaceutical formulations and human urine is responsive and transparent. The proposed approach could be used in clinical experiments and pharmacokinetics, including in complex matrix systems like drug preparations, due to its low identification and qualitative limitations compared to recently published research using costly electrodes.

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