MEDWIN PUBLISHERS
Committed to create value for Researchers

Advances in Pharmacology and Clinical Trials
ISSN: 2474-9214

DNA Binding Potential and Antibacterial Activity of Metamizole

Mostafa Norizadeh Tazehkand*

Pharmaceutical Biotechnology Department, Faculty of Pharmacy, Zonguldak Bulent Ecevit University, Zonguldak, Turkey

***Corresponding author:** Mostafa Norizadeh Tazehkand, Pharmaceutical Biotechnology Department, Faculty of Pharmacy, Zonguldak Bulent Ecevit University, Zonguldak, Turkey, Tel: +90 5372891027; Email: mostafa_noorizadeh@yahoo.com

Research Article

Volume 5 Issue 1

Received Date: December 09, 2019

Published Date: January 08, 2020

DOI: 10.23880/apct-16000172

Abstract

Metamizole is an anti-inflammatory medicine that is using in spasm, painkiller, reliever. The drug is using from a lot of people but there is a paucity of study about the antimicrobial and DNA binding activity of Metamizole. This study was aimed to investigate the antimicrobial (against *Escherichia coli* and *Enterococcus faecalis*) and DNA binding activity (on PUC18 Plasmid DNA) of Metamizole.

The result of this study showed that Metamizole does not have antibacterial effect on *Escherichia coli* and *Enterococcus faecalis*, because both bacterial strain were grown at all concentrations (0.049 to 12.5 mg/ml). The electrophoretic pattern of DNA treated with Metamizole (concentrations of 250, 125 and 62.5 µg) showed same bands on agarose gel as negative control. Therefore Metamizole did not break the PUC18 vector DNA.

It can be concluded that Metamizole might not pose a potential risk for our life. However, it must be investigated in other test systems.

Keywords: Metamizole; Antibacterial; DNA Binding; PUC18

Abbreviations: COX: Cyclooxygenase; DNA: Deoxyribonucleic Acid; E.Coli: Escherichia Coli; MIC: Minimum Inhibitory Concentration; MBC: Minimum Bactericidal Concentration; NSAID: Nonsteroidal Anti-Inflammatory Drugs; PUC18: Prefix (Plasmid) for The University Of California

Introduction

Prostaglandins promote inflammation that is important for healing, but also results in fever and pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) block the activity of COX and reduce the synthesis of prostaglandins in cells. Consequently reduce the inflammation, fever and pain [1]. Metamizole is one of anti-inflammatory drug that is in spasm, painkiller and reliever [2]. Metamizole was first used under the trade name "Novalgin" [3]. Metamizole is marketed under different brand names [4,5]. Metamizole can be taken parenterally or orally to therapy of postoperative pain, colic pain and acute injury pain [6]. Because Metamizole has a weak cyclo-oxygenase inhibitory effect, its use is not incorporated with gastric irritation, it is the best advantage for long-

term administration. Also, Metamizole has an intrinsic spasmolytic activity. This provides the drug particularly useful in renal colic pain [7]. Metamizole breaks down to pyrazolone compounds immediately after oral administration. It has some side effect, the most critical of risk is myelotoxic effect of this drug. Despite no evidence showing the risk of teratogenic and embryotoxic effects, the drug must not be used by pregnant women [8]. There is not any research about antibacterial and genotoxic effects of Metamizole. The aim of this study was to specify the effects of Metamizole on DNA breaking. This study also investigated the antibacterial effects of Salgam against *E.coli* as a gram neative bacteria and *Enterococcus faecalis* as a gram positive bacterial strain.

Material and Methods

In this study, the test substance, Metamizole, was purchased from *Adeka İlaç* and its properties and molecular structure is shown in Figure 1.

CAS ID: 68-89-3
Molar mass: 333.341 g/mol
Formula: $C_{13}H_{17}N_3O_4S$
Excretion: Urine (96%, IV; 85%, oral), faeces (4%, IV).
Bioavailability: 100% (active metabolites)
Trade name: Metamizole, dipyrone, Novalgin, others

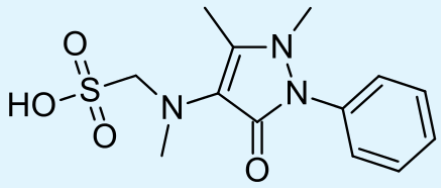

Figure 1: The structure of Metamizole.

Bacterial Strains

The test bacteria used in this study were from Bulent Ecevit University Medical Microbiology lab. *Enterococcus faecalis* ATCC 51299 as a gram positive bacteria and *Escherichia coli* ATCC 25922 as a gram negative bacteria. The bacterial strains were cultured in viable state via inoculation on Mueller-Hinton Broth and overnight incubation at 37°C.

Antimicrobial Activity of Metamizole

Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of Metamizole were determined by dilution method. Different concentrations of Metamizole (final concentrations of 0.049 to 12.5 mg/ml) were prepared and added to different tubes with 4 ml Mueller-Hinton Broth medium. So, a microbial suspension of 0.5 McFarland was obtained from two bacterial strains (*Enterococcus faecalis* ATCC 51299 as a gram positive bacteria and *Escherichia coli* ATCC 25922 as a gram negative bacterium) and the bacterial strains were cultured in prepared Mueller-Hinton Broth medium containing different Metamizole concentrations tubes. The tubes were then incubated at 37°C for overnight. The tube with the lowest concentration of the Metamizole at which no visible growth was reported as the MIC of the tested bacteria. The tubes were shaken to homogenize the contents and 100 µL of the contents of each tube was sub cultured by spreading Mueller-Hinton agar plastic petri dishes. The plates were incubated for 24 hours and then observed for any growth of colonies. Minimum bactericidal concentration was determined as the lowest concentration of Metamizole at which no colony observed following the sub culturing onto Mueller Hinton agar mediums [9-11].

DNA Binding Activity of Metamizole

DNA breaking potential of Metamizole was evaluated on PUC18 plasmid vector. The experiments were done in a volume of 8 µl in a microfuge tube containing 5 µl PUC18 (50µg/ml) plasmid DNA, and 5 µl of Metamizole in the concentrations of 250, 125 and 62.5 µg, respectively. In this research, untreated controls (PUC18 DNA) were also used. The reactions were incubated at 37°C temperature for 30 min. After incubation, the reaction mixture along with gel loading dye (6×) was loaded on a 2 % agarose gel for electrophoresis [12].

Result and Discussion

Antibacterial Activity of Metamizole

Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of Metamizole were determined by dilution method. In this research we tested *Enterococcus faecalis* ATCC 51299 as a gram positive bacteria and *Escherichia coli* ATCC 25922 as gram negative bacteria. The result obtained from this research showed that Metamizole has no antibacterial effect on *Enterococcus faecalis* and *Escherichia coli*, because both bacterial strains were grown at all tested concentrations. For this reason we cannot report MIC and MBC for Metamizole against *Enterococcus faecalis* and *Escherichia coli* (Figure 2 & 3).

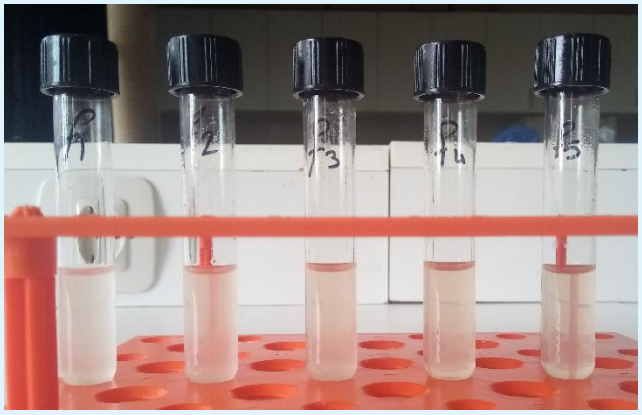

Figure 2: MIC result of *Enterococcus faecalis* ATCC 51299. 1: 12.5 mg/ml, 2: 6.25 mg/ml, 3: 3.125 mg/ml, 4: 1.56 mg/ml, 5:0.781 mg/ml. Metamizole could not inhibited the growing of *Enterococcus faecalis.*

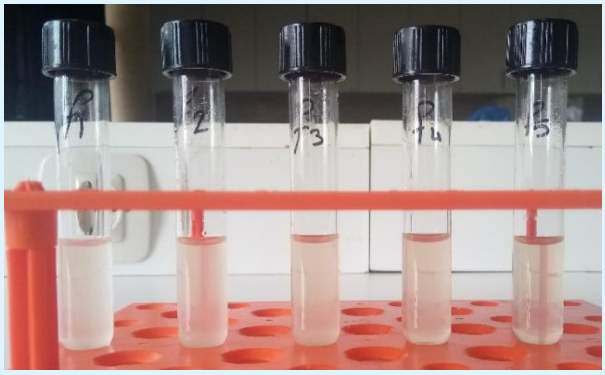

Figure 3: MIC result of *E. coli* ATCC 25922. 1: 12.5 mg/ml, 2: 6.25 mg/ml, 3: 3.125 mg/ml, 4: 1.56 mg/ml, 5:0.781 mg/ml. Metamizole could not inhibited the growing of *E. coli.*

DNA Breaking Activity of Metamizole

As it was shown in Figure 4, the electrophoretic pattern of DNA treated with Metamizole (concentrations of 250, 125 and 62.5 µg) showed same bands on agarose gel electrophoresis as untreated control. Therefore Metamizole did not break the plasmid DNA.

The results of this study showed that Metamizole has not antibacterial effect on *Enterococcus faecalis* and *Escherichia coli*. According to our knowledge, it was the first study that addresses the antibacterial effects Metamizole against *Enterococcus faecalis* and *Escherichia coli*. The results obtained from PUC18 plasmid DNA damaging assay showed that Metamizole has no genetoxic effect on PUC18 DNA, because the electrophoretic pattern of PUC18 DNA after Metamizole treatment showed same bands on agarose gel electrophoresis as untreated control. In our life some time we use different drugs for pain relief. Some of these drugs have genotoxic or antibacterial effects, for this reason we need to study about these substances.

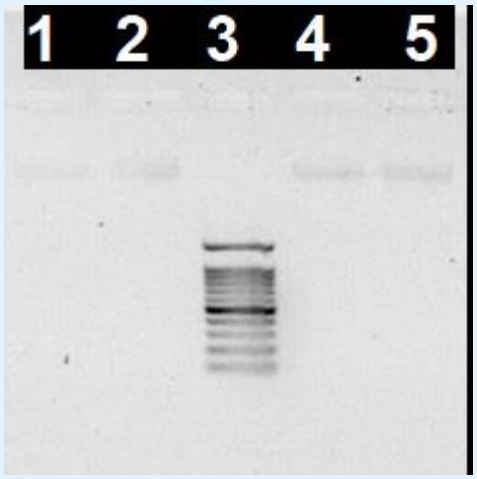

Figure 4: Electrophoretic pattern of PUC18 DNA after treatment with Metamizole. Lane 1: PUC18 DNA (untreated control); Lane 2: PUC18 treated with 62.5 µg of Metamizole; Lanes 3: Marker DNA. Lane 4: PUC18 treated with 125 µg of Metamizole; Lanes 5: PUC18 treated with 250 µg of Metamizole.

In contrast to Metamizole, number of reviews concerning the genotoxic property of some other pain relief drugs has been published. For example Oliván, et al. [13] showed that Diclofenac, ibuprofen and naproxen were responsible of alterations in biochemical biomarkers evaluated and DNA damage.

In another study the researchers reported that prolonged use of Diclofenac sodium at high doses is genotoxic in both somatic cells as well as the germinal cells of mice. Other experimental research reported that some of NSAIDs drugs provide antimicrobial properties against different bacterial strains. Bakri, et al. [15] reported that Aspirin have antibacterial effect on *P. aeruginosa* ATCC 9027 and *E. coli* ATCC 8739. Milani, et al. [16] investigated the antimicrobial activity of diclofenac and ibuprofen on *E. faecalis*. In accordance with this result, Milani, et al. [16] diclofenac and ibuprofen have significantly more pronounced antibacterial activity against *E. faecalis.*

Conclusion

The result of our research showed that Metamizole don't have antimicrobial and genotoxic effect. It can be concluded that Metamizole might not pose a potential risk for our life. However, it must be investigated in other test systems.

Acknowledgments

This study was funded by Zonguldak Bulent Ecevit University Research Fund (Zonguldak Bulent Ecevit University- BAP) 2018-27095600-02.

References

1. Ricciotti E, Fitz Gerald GA (2011) Prostaglandins and Inflammation. Arterioscler Thromb Vasc Biol 31(5): 986-1000.

2. Jage J, Laufenberg-Feldmann R, Heid F (2008) Drugs for postoperative analgesia: routine and new aspects. Part 1: non-opioids. Der Anaesthesist (in German) 57(4): 382-390.

3. United Nations Department of Economic and Social Affairs (2005) Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted of Not Approved by Governments (PDF) 12th (Edn.) New York: United Nations pp: 171-175.

4. Drugs.com (2015) International listings for Metamizole Page accessed.

5. Brayfield A (2013) Martindale: The Complete Drug Reference. Pharmaceutical Press.

6. Miljkovic MN, Rancic NK, Simic RM, Dusica M, Stamenkovic DM, et al. (2018) Metamizole: Current Status of the Safety and Efficacy. Hospital Pharmacology 5(3): 694-704.

7. Konijnenbelt PJ, van der HC, Ekhart C, Bos J, Bruhn J, Kramers C, et al. (2017) Metamizole (Dipyrone) as an Alternative Agent in Postoperative Analgesia in Patients with Contraindications for Nonsteroidal Anti-Inflammatory Drugs. Pain Pract 17(3): 402-408.

8. Jasiecka A, Maślanka T, Jaroszewski JJ (2014) Pharmacological characteristics of metamizole. Pol J Vet Sci 17(1): 207-214.

9. Norizadeh M, Hajipour O (2017) Antibacterial effect of brilliant blue food dye. IJMCM 7(2). 890-895.

10. Norizadeh Tazehkand M (2018) The investigation of anti-bacterial activity of Reactive Red-120. J Pharmacol Med Chem 2(1): 1-3.

11. Norizadeh tazehkand M, Valipour E (2019) Cytotoxic, antimicrobial and DNA breaking activity of Salgam. IJBB 56(2): 169-174.

12. Tazehkand MN, Moridikia A, Hajipour O, Valipour E, Timocin T, ET AL. (2016) The effects of 4-MEI on cell proliferation, DNA breaking and DNA fragmentation. Bratislavske Lekarske Listy 117(7): 371-375.

13. Gómez Oliván LM, Galar Martínez M, García Medina S, Valdés Alanís A, Islas Flores H, et al. (2014) Genotoxic response and oxidative stress induced by diclofenac, ibuprofen and naproxen in Daphnia magna. Drug Chem Toxicol 37(4): 391-399.

14. Tripathi Rina, Tripathi Pankaj, Pancholi SS (2014) Genotoxicity Studies of Diclofenac Sodium in the Bone Marrow and Germ cells of Laboratory Mice. Austin J Pharmacol Ther 2(10): 1054.

15. Al-Bakri AG, Othman G, Bustanji Y (2009) The assessment of the antibacterial and antifungal activities of aspirin, EDTA and aspirin-EDTA combination and their effectiveness as antibiofilm agents. J Appl Microbiol 107(1): 280-286.

16. Salem Milani A, Balaei Gajan E, Rahimi S, Moosavi Z, Abdollahi A, ET AL. (2013) Antibacterial Effect of Diclofenac Sodium on Enterococcus faecalis. J Dent 10(1): 16-22.