



Antibacterial Activity of Paracetamol, Trimethoprim/sulfamethoxazole, Azithromycin, and Ciprofloxacin

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Article History	Abstract
Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 25 Nov 2023	<p><i>Paracetamol have indirect antibiotic activity and are commonly coadministered with antimicrobial therapy. This study aimed to assess the synergistic effect of Paracetamol to with Azithromycin, Trimethoprim/sulfamethoxazole and Ciprofloxacin against salmonella and Escherichia coli. In this study, Ciprofloxacin, Trimethoprim/sulfamethoxazole and Azithromycin was mixed paracetamol against salmonella and Escherichia coli. The results showed that the interaction between Paracetamol and Azithromycin, Trimethoprim/sulfamethoxazole and ciprofloxacin exhibited more in inhibitory potency against on Gram-negative salmonella and Escherichia coli. The combinations of Paracetamol with the Azithromycin and Trimethoprim/sulfamethoxazole showed significant inhibitory activity on the salmonella and Escherichia coli comparing to the inhibition activity showed from the tested antibiotics alone.</i></p>
CC License CC-BY-NC-SA 4.0	<p>Keywords: Paracetamol, Trimethoprim/sulfamethoxazole, Azithromycin, Ciprofloxacin antibacterial activity</p>

1. Introduction

Acetaminophen or paracetamol chemically name N-acetyl-p-aminophenol is one of the most commonly used analgesic and anti-pyretic agents for alleviating acute and chronic pain. Due to its safety, acetaminophen is prescribed for patients in whom non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated, such as those with gastric ulcers and bronchial asthma, pregnant women, nursing mothers, and children (Leung, 2012; Roberts et al., 2016). It is typically used for mild to moderate pain.

Paracetamol is part of the class of drugs known as "aniline analgesics". (Hanel and Lands 1982). It does not have significant anti-inflammatory activity and how it works is not entirely clear (Zainab R. Abdul-Hussein, 2014). Paracetamol have indirect antibiotic activity and are commonly coadministered with antimicrobial therapy, it is important to understand the interactions between these two classes of drugs (Zainab R Abdul-Hussein 2018). This project had the following objectives with the hypothesis that the combinational therapy of an antibiotic and an Acetaminophen agent is viewed as an adjuvant molecule presents a viable therapeutic alternative to treat infections and inflammatory conditions.

2. Materials And Methods

This study, is based on evaluating the effectiveness of Acetaminophen or paracetamol in combination with some antibiotics against several strains of bacteria.

Tested Drugs:

Azithromycin (AZM-15), Ciprofloxacin (CIP-5), Trimethoprim/sulfamethoxazole (SXT-25) and Paracetamol (B.P.2016-ADWIC).

Tested Bacteria:

Escherichia coli and *Salmonella typhimurium*.

Preparation of bacterial sample:

Two isolates of Gram stain negative bacteria were included in this study, (*Escherichia coli* and *Salmonella typhimurium*) both bacteria were obtained from private laboratory in Shahat city.

Antibacterial Assay:

Ciprofloxacin, Trimethoprim/sulfamethoxazole and Azithromycin put on nutrient agar medium plates, which their surfaces were previously streaked separately with tested *E.Coli* and also Ciprofloxacin, Trimethoprim/sulfamethoxazole and Azithromycin put on nutrient agar medium plates, which their surfaces were previously streaked separately with tested *Salmonella typhimurium*. The same procedures were done for tested paracetamol.

All plates were incubated at 37C° for 24 hours. After 24 hours the inhibition zones were measured in (mm) unit.

Assay of combinational effect of Paracetamol, Azithromycin, Ciprofloxacin and Trimethoprim/sulfamethoxazole

Each Ciprofloxacin, Trimethoprim/sulfamethoxazole and Azithromycin was mixed paracetamol put on nutrient agar medium plates, which their surfaces were previously streaked separately with tested *E.Coli* and also Ciprofloxacin, Trimethoprim/sulfamethoxazole and Azithromycin was mixed paracetamol put on nutrient agar medium plates, which their surfaces were previously streaked separately with tested *Salmonella typhimurium*.

All plates were incubated at 37C° for 24 hours. After 24 hours the inhibition zones were measured in (mm) unit.

3. Results and Discussion

In this study, results of antibacterial represent in The following Figures 1-4. When antibacterial Activity of Azithromycin+paracetamol, Ciprofloxacin alone, Ciprofloxacin +paracetamol and paracetamol alone on *Escherichia coli*, the results revealed that active performance against the tested bacteria; with mean of inhibition zones of 20 mm, 21 mm, 22 mm and 16mm, respectively. In addition Azithromycin no found any activity against *Escherichia coli* (figure 1).



Fig. 1: Antibacterial Activity of Azithromycin alone, Azithromycin+paracetamol, Ciprofloxacin alone, Ciprofloxacin +paracetamol and paracetamol alone on *Escherichia coli*

In other assay where a combination Trimethoprim/sulfamethoxazole +paracetamol had done and investigated for the antibacterial activity, the results showed inhibition zones of mean of 25mm against *Escherichia coli* (figure 2).



Fig. 2: Antibacterial Activity of Trimethoprim/sulfamethoxazole alone and Trimethoprim/sulfamethoxazole +paracetamol on *Escherichia coli*

In a next step the antibacterial activity of Trimethoprim/sulfamethoxazole alone, Trimethoprim/sulfamethoxazole+ paracetamol, Ciprofloxacin alone and Ciprofloxacin +paracetamol against both *Salmonella* was investigated and the result showed growth inhibition zones of mean of 25 mm, 27 mm, 23 mm and 23 mm respectively (figure 3).

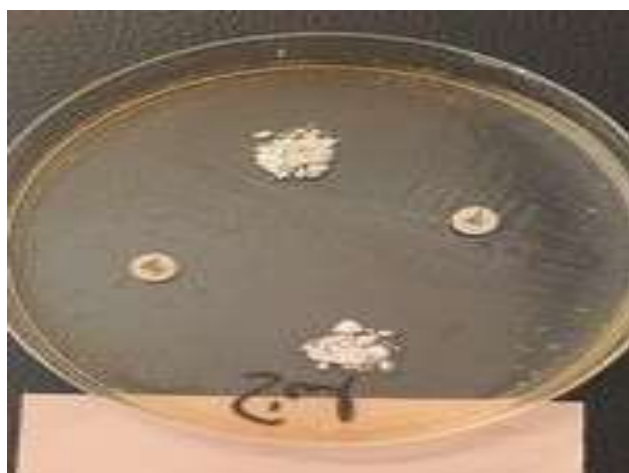


Fig. 3: Antibacterial Activity of Trimethoprim/sulfamethoxazole alone, Trimethoprim/sulfamethoxazole+paracetamol, Ciprofloxacin alone and Ciprofloxacin +paracetamol on *Salmonella*

In addition, this study assessed the antibacterial activity Azithromycin alone, Azithromycin+paracetamol and paracetamol alone, the results showed inhibition zones of mean of 42mm against 22mm, 25 mm and 13mm respectively against *Salmonella* (figure 4).



Fig. 4: Antibacterial Activity of Azithromycin alone, Azithromycin+paracetamol and paracetamol alone on *Salmonella*

Table1: Antibacterial Activity of Tested Drugs on *Escherichia coli* and *Salmonella*.

Tested Drugs	Mean of Diameter of Inhibition Zones (IZ) in Millimeter Against Tested Bacteria	
	<i>Escherichia coli</i>	<i>Salmonella</i>
paracetamol	16	13
Azithromycin	0	22
Azithromycin+ paracetamol	20	25
Ciprofloxacin	21	23
Ciprofloxacin+ paracetamol	22	23
Trimethoprim/sulfamethoxazole	0	25
Trimethoprim & sulfamethoxazole+ paracetamol	25	27

1-Antibacterial activity of paracetamol

In this study, paracetamol was tested separately for their antibacterial activity and showed antibacterial activity against *salmonella* Gram-negative, flagellated facultatively anaerobic bacilli bacterium and *Escherichia coli* Gram-negative, facultative anaerobic, rod-shaped, coliform bacterium.

Paracetamol, the most widely used are reported to improve the performance of antibiotics either through their synergistic antibacterial action with antibiotics or by reducing adherence, production of biofilm, and other virulence factors as well as by altering pathogen susceptibility to antibiotics. (Singh et al, 2021).

Paracetamol and/or non-steroidal anti-inflammatory drugs (NSAIDS) are of use for symptomatic relief. However, recent research suggests that some NSAIDs may also have the capacity to treat UTI caused by *E. coli* (Mazumdar K, Dutta NK. et al 2007). The effect of acetaminophen on the susceptibility of *Pseudomonas aeruginosa* against antibiotic was less significant than urinary tract bacteria.

2-Antibacterial activity of paracetamol in combination with Azithromycin, Trimethoprim/sulfamethoxazole and Ciprofloxacin

Up to date of this study, no study found done to determine the synergistic effects of paracetamol with Azithromycin, Trimethoprim/sulfamethoxazole, Ciprofloxacin against *salmonella* and *Escherichia coli*. This study is the first study investigate if there is any synergistic effect between the above-mentioned drugs, and it revealed interesting evidence where it proved that the combination of Azithromycin, Trimethoprim/sulfamethoxazole, ciprofloxacin and Paracetamol have a good synergistic effect on *salmonella* and *Escherichia coli*, where it clarified that the antibacterial activity of paracetamol with Azithromycin, Trimethoprim/sulfamethoxazole combination is stronger than that given from Azithromycin and Trimethoprim/sulfamethoxazole, alone.

These findings point to the possible adjuvant use of Azithromycin, Trimethoprim/sulfamethoxazole, ciprofloxacin and paracetamol in the treatment of *salmonella* and *Escherichia coli* infections.

4. Conclusion

This study conclude that paracetamol has a good synergistic effect with Azithromycin, Trimethoprim/sulfamethoxazole and ciprofloxacin against the Gram-negative *salmonella* and *Escherichia coli*, and it suggests that this combination could be considered as a good regimen to treat infection caused by these two species of pathogenic bacteria. In addition, this study recommends further studies to figure out the exact chemical reaction done between the tested antibiotic and paracetamol agents and stand behind this promising activity.

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