ACTA SCIENTIFIC MICROBIOLOGY (ISSN: 2581-3226)

Volume 3 Issue 8 August 2020

Research Article

To Assess the Antimicrobial Action of Paracetamol

Dr Anita K Verma[1], Disha Mittal[2], Ayushi Goel*[2], Lakshay Shadija[2] and Nisha Singh[2]

[1]Kirori Mal College, Department of Zoology, University of Delhi, India

[2]Department of Zoology, University of Delhi, India

***Corresponding Author:** Ayushi Goel, Department of Zoology, University of Delhi, India.

Received: June 24, 2020

Published: July 25, 2020

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Abstract

Paracetamol is the most commonly used mild analgesic. It is easily accessible and is widely used worldwide to treat common ailments like pain and fever. Previous studies have shed light on the hepatotoxicity associated with Paracetamol overdose and hinted at its ties to the enzyme Cyclooxygenase which it inhibits to alleviate Prostaglandin synthesis and hence pain. However, little research has been done on its pharmacokinetics and pharmacomicrobiomics. The exact mechanism of action of Paracetamol still remains a mystery and little is known about its effect on the gut flora, if any. In this paper, we briefly assess the antimicrobial activity of Paracetamol.

Keywords: Acetaminophen; Antimicrobial; Analgesic; Crocin; Cyclooxygenase; Escherichia coli; Staphylococcus aureus; Paracetamol; Prostaglandins

Abbreviations

APAP: Acetaminophen; COX: Cyclooxygenase; CNS: Central Nervous System; *E. coli*: *Escherichia coli;* NSAIDS: Non-Steroidal Anti-Inflammatory Drugs; PG: Prostaglandin; *S. aureus*: *Staphylococcus aureus*

Introduction

Paracetamol is the most commonly used analgesic and antipyretic in both the United States and Europe. It is on the WHO Model List of Essential Medicines. Paracetamol is available as a generic medication with trade names including Tylenol, Panadol, Crocin and several others.

Crocin is the Indian brand name of paracetamol. Paracetamol, also known as Acetaminophen or APAP. It is typically used for mild to moderate pain. It does not have significant anti-inflammatory activity and how it works is not entirely clear.

Acetaminophen is thought to act primarily in the CNS, increasing the pain threshold by inhibiting both isoforms of Cyclooxygenase, COX-1 and COX-2, enzymes involved in prostaglandin (PG) synthesis.

The prostaglandins (PG) are a group of physiologically active lipid compounds having diverse hormone-like effects in animals. They are derived enzymatically from fatty acids and act on an array of cells. They exhibit a wide variety of effects such as - aggregation or disaggregation of platelets, sensitize spinal neurons to pain, induce labor, regulate inflammation and hormones and control cell growth. They also act on the thermoregulatory center of the hypothalamus to produce fever and on parietal cells in the stomach wall to inhibit acid secretion.

Unlike NSAIDS, Acetaminophen does not inhibit Cyclooxygenase peripherally. While aspirin acts as irreversible inhibitors of COX and directly blocks the enzyme's active site, studies have found that acetaminophen indirectly blocks COX and that this blockage is ineffective in the presence of peroxides. This might explain why acetaminophen is effective in the central nervous system and in endothelial cells but not in platelets and immune cells which have high levels of peroxides. Studies also report data suggesting that acetaminophen selectively blocks variants of COX enzyme that are different from the known variants COX-1 and COX-2. This enzyme is now referred to as COX-3.

Its exact mechanism of action is still poorly understood and our study aims to delineate a different property of Paracetamol which has not been studied so far. Assessment of its antimicrobial activity may ward off us against its overuse in medical practice and as an over the counter medicine.

Materials and Methods

Bacterial cultures: *E. coli* and *S. aureus.*

Drugs: Crocin Advance 500 mg, Crocin Pain Relief 650 mg.

Spreading of bacterial culture

2 ul of bacterial culture was mixed with 3 ml of soft agar in petri dishes and spreaded over the hard agar.

Preparation of Crocin Advance 500 mg and Crocin Pain Relief 650 mg solutions

Three replicates of varying concentrations were taken for each drug. Paracetamol concentrations were as follows - 200 mg/ml, 400 mg/ml, and 600 mg/ml. The drugs were dissolved in 0.5 ml water in each eppendorf.

Disc diffusion assay

1 mg/ml Gentamicin was used as a positive control and distilled water was used as a negative control. Whatman Antibiotic Assay 6 mm discs were dipped in the respective drug solutions and placed on the corresponding sections. The petri dishes were sealed with parafilm and kept at 37°C overnight. They were observed the next morning and the zone of inhibition was measured.

Results

Paracetamol or Acetaminophen possesses mild antimicrobial properties *in vitro*.

Crocin pain relief has more antimicrobial properties than crocin advance.

E. coli is more sensitive than *S. aureus* towards the antimicrobial activity of Paracetamol.

Bacteria					
S. aureus			***E. coli***		
Sample	**Conc. of antibiotic (mg/ml)**	**Z.O.I (mm)**	**Sample**	**Conc. of antibiotic (mg/ml)**	**Z.O.I (mm)**
Gentamicin	1	7	Gentamicin	1	9
Distilled water	0	0	Distilled water	0	0
C.A.	200	<0.2	C.A.	200	<0.5
C.A	400	0.2	C.A.	400	1.5
C.A	600	1	C.A.	600	2
C.P.R.	200	0.25	C.P.R.	200	0.75
C.P.R.	400	0.5	C.P.R.	400	2.5
C.P.R.	600	1.5	C.P.R.	600	5

Table 1: Disc diffusion assay scores. C.A: Crocin Advance; C.P.R: Crocin Pain Relief; Z.O.I: Zone of Inhibition.

Discussion

Despite being one of the most widely used medicines in the world, debate continues over the exact mechanism of action of Paracetamol. The consensus suggests Paracetamol achieves its pharmacological effects by inhibiting Cyclooxygenase (COX) in the brain. COX is responsible for synthesis of Prostaglandins which are involved in inflammation and repair after injury. Therefore, COX inhibition reduces pain intensity and fever. This mechanism of pain alleviation is absent in microorganisms as they do not have this enzyme.

Since Paracetamol is one of the most commonly used and easily accessible drugs, testing its antimicrobial activity (if any) has long been an area of interest.

Paracetamol shows very mild antimicrobial activity and cannot be classified as an antimicrobial agent. However, it may lead to liver

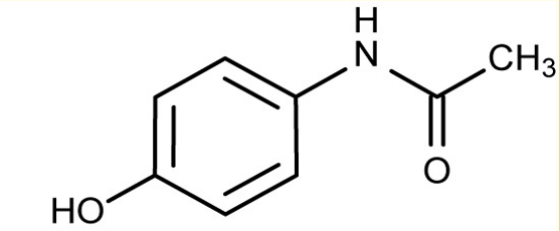

Figure 1: Structure of Acetaminophen.

Figure 2: Antimicrobial activity of Crocin Pain Relief against Gram positive bacteria (*S.aureus*) at various concentrations of acetaminophen

Figure 3: Antimicrobial activity of Crocin Advance 500 mg against *S.aureus* at various concentrations of acetaminophen.

Figure 4: Antimicrobial activity of Crocin Pain Relief - 650mg against *E.coli* at various concentrations of acetaminophen.

Figure 5: Antimicrobial activity of Crocin Advance 500 mg against *E.coli* at various concentrations of acetaminophen.

damage if overdosed, due to its high toxicity. It may also disrupt the composition and the diversity of the gut microbiome at a very high dosage.

Higher antimicrobial activity of Crocin Pain Relief as compared to Crocin Advance can be ascribed to the differences in their excipients.

E. coli was more susceptible to Paracetamol than *S. aureus*. This may be due to differences in their cell wall thickness. *E. coli* being a gram negative bacteria has a thinner cell wall than *S. aureus* which is a gram positive bacteria.

The proposed mechanism of action of Paracetamol on bacteria may be one of the following: creating pores in the cell membrane followed by cell lysis, binding to the DNA of the bacteria and damaging it, or inhibiting metabolic processes like folic acid synthesis that is a precursor of DNA synthesis.

Conclusion

Acetaminophen shows a mild antimicrobial effect on *S. aureus* and *E. coli in vitro*, but the results may vary in an *in vivo* environment. It is also highly dependent upon the concentration or the dosage of the drug administered. The antimicrobial activity increases linearly with the concentration of Paracetamol.

It may harm our gut flora at a very high dosage. Therefore, care should be take against overuse of Paracetamol and its dosage should be carefully monitored.

The mechanism of action of Paracetamol, however, still remains unclear, so further experiments can be done in this direction.

Acknowledgements

We are thankful to Dr. Anita K. Verma (Zoology Department, Kirori Mal College), for providing us with the opportunity to work on a research project under her guidance and supervision. We are very grateful to Ms. Disha Mittal (PhD Scholar) for the guidance and constant support she provided us with.

We have tried our best to present this information as clearly as possible in the hope that it will be comprehended by the widest spectrum of researchers, analysts and students for further studies.

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