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A Review on Paracetamol: Pharmacology, Uses and Toxicity

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ABSTRACT: One of the most widely used analgesic and antipyretic medications used in the management of pain and fever worldwide is Paracetamol (acetaminophen). Its efficacy, low cost, broad availability and relatively good safety profile when used within its recommended dosage makes it a first-line therapeutic option since its introduction into clinical practice. Contrary to non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol is an effective agent of mild to moderate pain relief, fever reduction, and none of the drugs has significant side effects on the gastrointestinal tract, platelets, or cardiovascular systems. This is particularly helpful when used with children, elderly patients, pregnant women due to medical supervision, and patients in whom NSAIDs are contraindicated. Pharmacologically, paracetamol acts primarily in the central nervous system by inhibiting the synthesis of prostaglandins hence giving it analgesic and antipyretic properties. It has little anti-inflammatory effect due to its low peripheral cyclooxygenase inhibition. Paracetamol is readily absorbed after oral administration, widely distributed and mainly metabolised in the liver by glucuronidation and sulfation pathways. Cytochrome P450 enzymes are able to convert a small proportion to a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI), which would otherwise be detoxified by glutathione. But when glutathione stores are depleted (either in overdose or in prolonged excessive use) glutathione accumulates in the body, leading to severe hepatocellular injury. One of the most common causes of acute liver failure in world and may occur as either an intentional overdose of paracetamol, a repeated high-dose of paracetamol or as an accidental ingestion of multiple combination products containing paracetamol. Serum drug level and treatment with N-acetylcysteine (NAC) is the key to preventing serious complications. This review discusses the pharmacology, mechanism of action, therapeutic uses, dosage, administration, toxicity, and management of paracetamol. It also notes major advantages of it like safety, accessibility, and tolerability, and major limitations of it such as hepatotoxicity and important lack of anti-inflammatory effects. Rational prescribing, patient education, and close monitoring are all fundamental in maximizing therapeutic benefits, and minimizing the risks associated with the use of this widespread drug.

KEYWORDS: Paracetamol, Acetaminophen, Analgesic, Antipyretic, Pharmacology, Pain management, Fever, Hepatotoxicity, NAPQI, Glutathione, Overdose, Liver failure, N-acetylcysteine, NSAIDs, Drug safety, Therapeutic uses, Dosage, Toxicity, Pharmacokinetics, Mechanism of action, Drug metabolism, Clinical practice, Patient safety, OTC medicine.

I. INTRODUCTION

Acetaminophen is a type of medication that is used in the majority of countries all over the world to manage pain and fever. Since its introduction in the clinical practice in the middle of the 20th century, paracetamol has become the first line therapeutic agent due to its effectiveness, cost-effectiveness, and relatively good safety profile when used at the recommended doses[1]. It can be found over-the-counter in most countries and can be found in many combination formulations, which further adds to its widespread use in a variety of populations[2]. Among the most frequent symptoms that are usually experienced in the clinical practice, pain and fever are among the most important symptoms that are usually dealt with to improve patient comfort and life[3]. In this respect, paracetamol is very important especially in that the drug offers effective analgesia of mild to moderate severity without the serious gastrointestinal and cardiovascular side effects usually caused by non-steroidal anti-inflammatory drugs (NSAIDs)[4]. It is not as effective as NSAIDs in anti-inflammatory activity, primarily because it has very little anti-inflammatory activity, but is much more effective in general analgesic and antipyretic practices. The appropriateness of using paracetamol in various categories of patients, including children, pregnant women (when under medical supervision), and elderly, is one of the primary reasons of why the use of paracetamol has gained widespread acceptance. Its safety profile when used within therapeutic limits has made it a preferential in situations where other analgesics may be contraindicated. Moreover,

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paracetamol also comes in different dosage forms such as tablets, syrups, suppositories, and intravenous preparations, which also allows some flexibility in its administration in relation to patient needs and clinical environments[5]. Pharmacologically, paracetamol, is an analgesic and antipyretic agent. Its mechanism of action is not fully understood but it is believed to have an effect on the central nervous system which is believed to inhibit the production of the prostaglandins which are known to increase pain perception and control the body temperature. In comparison with traditional NSAIDs, paracetamol has a weak inhibitory effect on peripheral cyclooxygenase (COX)-enzymes, which explains the lack of significant anti-inflammatory effects and reduced risk of causing gastric irritation[6]. Although paracetamol is a widely used drug, which is relatively safe, it is not risk-free. The possibility of hepatotoxicity in instances of overdose or chronic use of high doses is one of the most important issues related to its use. The liver is the major site of the metabolism of paracetamol, and under normal conditions the drug is mainly metabolized to non-toxic conjugates. But a small percentage of this is transformed to a highly reactive and toxic metabolite called N-acetyl-p-benzoquinone imine (NAPQI)[7]. In the therapeutic conditions, this metabolite is promptly de-toxified by glutathione. During overdose, the stores of glutathione become depleted causing the buildup of NAPQI and resultant damage to liver cells, which can cause acute liver failure[8]. Of specific interest is the problem of paracetamol toxicity due to its easy access and availability in various combination products, which raises the risk of accidental overdose. It is consequently necessary to provide proper patient education as well as public health awareness in order to achieve a safe usage. Nurse practitioners, particularly the pharmacists, are very crucial in advising the patients on how to take the medication, the possible risks, and the need to take the medication as recommended[9]. Over the last few years, there has been a growing interest in knowing the exact mechanism of action, how to optimize dosing schedules and how to improve the safety profile of paracetamol. Studies are still ongoing to determine its impact at the molecular level and its interaction with other drugs[10]. Moreover, the regulatory authorities have put up measures to restrict the maximum allowable doses and enhance labelling to minimize the occurrence of toxicity. This review seeks to offer a detailed discussion about paracetamol, its pharmacology, mechanism of action, therapeutic effects, and toxicity. The article aims to not only highlight the benefits and limitations of this widely used drug in clinical practice, but also highlight the importance of its rational and safe use in clinical practice.

II. PHARMACOLOGY OF PARACETAMOL

One of the most widely used analgesic and antipyretic drugs in contemporary medicine is paracetamol. Its pharmacological profile includes the facts of good pain- and fever-reduction, minimal anti-inflammatory activity and a relatively safe therapeutic index when used within recommended limits. To understand its pharmacology, one needs to study its classification, pharmacokinetics, as well as its metabolic routes which are all relevant to its clinical utility and safety[11].

2.1 Classification

Paracetamol is an antipyretic and analgesic drug that is a non-opioid medication. It does not cause sedation, respiratory depression or dependence, unlike opioid analgesics, making it a less dangerous option when managing routine pain. It is also dissimilar to non-steroidal anti-inflammatory drugs (NSAIDs) since it portrays very weak anti-inflammatory characteristics. Pharmacologically paracetamol is occasionally classified in the same group as NSAIDs because it has the capacity to inhibit the production of prostaglandins[11]. Nevertheless, this classification cannot be considered as entirely accurate since it does not have any significant peripheral anti-inflammatory effects and lacks any strong peripheral inhibitory cyclooxygenase enzymes[12]. Rather, it has a more intense action in the central nervous system. These properties have led to the perception that paracetamol is a centrally acting analgesic, which explains why paracetamol is particularly useful in the treatment of headaches, mild musculoskeletal pain and fever. Its special classification enables it to be used as an alternative in patients who cannot afford NSAIDs because of gastrointestinal irritation, chance of bleeding, or hypersensitivity[13].

2.2 Pharmacokinetics

Pharmacokinetics of paracetamol: The absorption, distribution, metabolism and excretion of paracetamol in the human body is explained by pharmacokinetics. These mechanisms dictate how, when and how long its therapeutic effects will last[14].

Absorption

When given orally, paracetamol is rapidly and near-complete absorbed through the gastrointestinal tract. The maximum plasma concentrations are usually reached within 30 minutes to 2 hours, depending on the formulation and the gastrointestinal emptying. Food may slightly retard the rate of absorption, but does not as a rule affect the overall extent

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of absorption. Besides administration orally, paracetamol may also be administered by intravenous and rectal routes. I.V., offers a quicker onset of activity, making it applicable in acute care situations, with rectal administration being commonly applied in pediatric patients or in cases where oral administration is not possible[15].

Distribution

After being absorbed, paracetamol is evenly distributed in the majority of body tissues and fluids. Its plasma protein binding is rather low (around 1025%), which implies that a huge percentage of the drug is left unbound and pharmacologically active. Paracetamol can cross the blood-brain barrier, and therefore can exert its central analgesic and antipyretic effects. It is also able to pass through the placenta and is present in breast milk though in most cases in very low concentrations and this is considered safe under normal therapeutic conditions[16].

Onset and Duration of Action.

Analgesic effects usually take place within 30-60 minutes following oral intake, and the maximum effects are achieved in 1-3 hours. Onset time is normally 4-6 hours and this is the reason why the dosing time is usually 4-6 hours.

Elimination

The approximate half-life of paracetamol in healthy adults is 2-3 hours. This can be however extended in instances of liver impairment, overdose or in neonates because of immature metabolic pathways. The excretion of paracetamol and its metabolites is mainly through the kidney in urine with major percentage of the drug being excreted within 24 hrs[17].

Metabolism

The liver is the most important site of paracetamol metabolism and this is the main process in its therapeutic action and potential toxicity. In healthy individuals, paracetamol is broken down in three major routes:

1. Glucuronidation (Major Pathway): Conjugation with glucuronic acid to form non-toxic metabolites is the metabolic pathway of about 5060% of the paracetamol intake. They are water-soluble and can be readily excreted in urine[18].
2. Sulfation (Major Pathway): The other 2535 percent of the drug is sulphated and forms sulphate conjugates which are also non-toxic and readily excreted[19].
3. Cytochrome P450 Pathway (Minor yet Critical): The percentage of paracetamol that is metabolized by hepatic cytochrome P450 enzymes, especially CYP2E1, to produce a highly reactive and toxic intermediate NAPQI (N-acetyl-p-benzoquinone imine). In normal therapeutic conditions, NAPQI is quickly detoxified by conjugating with glutathione, a naturally occurring antioxidant in the liver forming harmless compounds which are excreted in the urine[20].

The action of Glutathione in Detoxification: Glutathione is essential in counterbalancing NAPQI and preclinically inhibit cell damage. The toxic metabolite does not accumulate, and the drug is safe as long as the levels of glutathione are maintained[21]. Nevertheless, the main metabolic pathways (glucuronidation and sulfation) are oversaturated in the cases of paracetamol overdose. Consequently, it causes a redistribution of the drug towards the cytochrome P450 pathway, resulting in a bigger production of NAPQI. Meanwhile, the glutathione storage facilities get depleted, which negatively affects the detoxification process. This causes accumulation of NAPQI which binds to cellular proteins resulting in oxidative stress and ultimately causes hepatocellular injury and liver necrosis[21].

Factors Affecting Metabolism:

The metabolism and toxicity of paracetamol can be influenced by several factors:

- Chronic alcoholism: This causes CYP2E1 enzyme activity which enhances the formation of NAPQI.
- Malnutrition: Decreases glutathione, which is necessary to detoxify.
- Liver disease: Reduces metabolic ability.
- Drug interactions: Some drugs are able to activate or inhibit cytochrome P450 enzymes.

The factors have the capability of elevating the risk of toxicity even in low doses that are otherwise assumed to be safe[22].

Overview of Pharmacological Profile.

- Paracetamol's pharmacology is defined by:
- Quick absorption and action.
- Good central analgesic and antipyretic action.

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- Extensive hepatic metabolism
- Normal elimination that is safe.
- Risk of extreme toxicity in overdose, because of the development of NAPQI[23].

Parameter	Description
Absorption	Rapid and almost complete absorption from the gastrointestinal tract after oral administration
Peak Plasma Concentration	Reached within 30 minutes to 2 hours
Effect of Food	May delay absorption slightly but does not significantly affect total absorption
Distribution	Evenly distributed in most body tissues and fluids
Plasma Protein Binding	Low (approximately 10–25%)
Blood-Brain Barrier	Crosses BBB and produces central analgesic and antipyretic effects
Placental Transfer	Crosses placenta and appears in breast milk in low concentration
Half-life	Approximately 2–3 hours in healthy adults
Elimination	Mainly excreted through kidneys in urine
Duration of Action	Usually lasts 4–6 hours

III. MECHANISM OF ACTION

The mechanism of action of Paracetamol is not fully understood, but is mostly known to act within the central nervous system (CNS) to bring about analgesic (pain-relieving) and antipyretic (fever-reducing) effects. In contrast to non-steroidal anti-inflammatory drugs (NSAIDs), which act primarily in the peripheral tissues, paracetamol has rather a central mode of action[24]. One of the most important processes is the fact that the production of prostaglandins in the brain is inhibited. Chemical intermediates known as prostaglandins are very important in the development of pain and fever. They are generated by the action of the enzyme Cyclooxygenase (COX), especially COX-2 which is produced during the inflammatory and febrile conditions[25]. Paracetamol blocks this enzyme in CNS resulting in the inhibition of the formation of prostaglandins and, as a consequence, the perception of pain and a decrease in body temperature. Paracetamol has effects on the hypothalamus, which is the thermoregulatory centre of the brain. Pyrogens provoke the synthesis of prostaglandins in the hypothalamus, increasing the temperature set point in the body. Paracetamol lowers this high set point by inhibiting the production of prostaglandins, promoting the loss of heat to the environment by vasodilation and sweating and ultimately returning the normal body temperature. A further proposed mechanism is that paracetamol may selectively inhibit a form of the cyclooxygenase enzyme that is sometimes referred to as COX-3 which is believed to be more dominant within the CNS. Even though this theory is still controversial, it supports the fact that paracetamol has little anti-inflammatory effects in peripheral tissues. Besides its action on the prostaglandins, paracetamol can also implicate other central pathways[26]. It has also been proposed that it increases the activity of descending serotonergic pathways that regulate pain messages thereby facilitating its analgesic effect. Moreover, other studies show that the metabolites of paracetamol may interact with endocannabinoid system which is involved in pain control and mood regulation. In contrast to NSAIDs, paracetamol has no significant effect on the expression of prostaglandins in peripheral tissues[27]. This is why it does not have strong anti-inflammatory effects and does not cause all typical side effects of NSAID used like gastric irritation or platelet inhibition. Consequently, paracetamol is mostly favoured in patients who are at risk of gastro intestinal complications. In general, the mechanism of action of paracetamol is complicated and includes numerous pathways, mainly in the central nervous system. It is a special and popular therapeutic agent because of its capability to decrease pain and fever with minimal peripheral effects[28].

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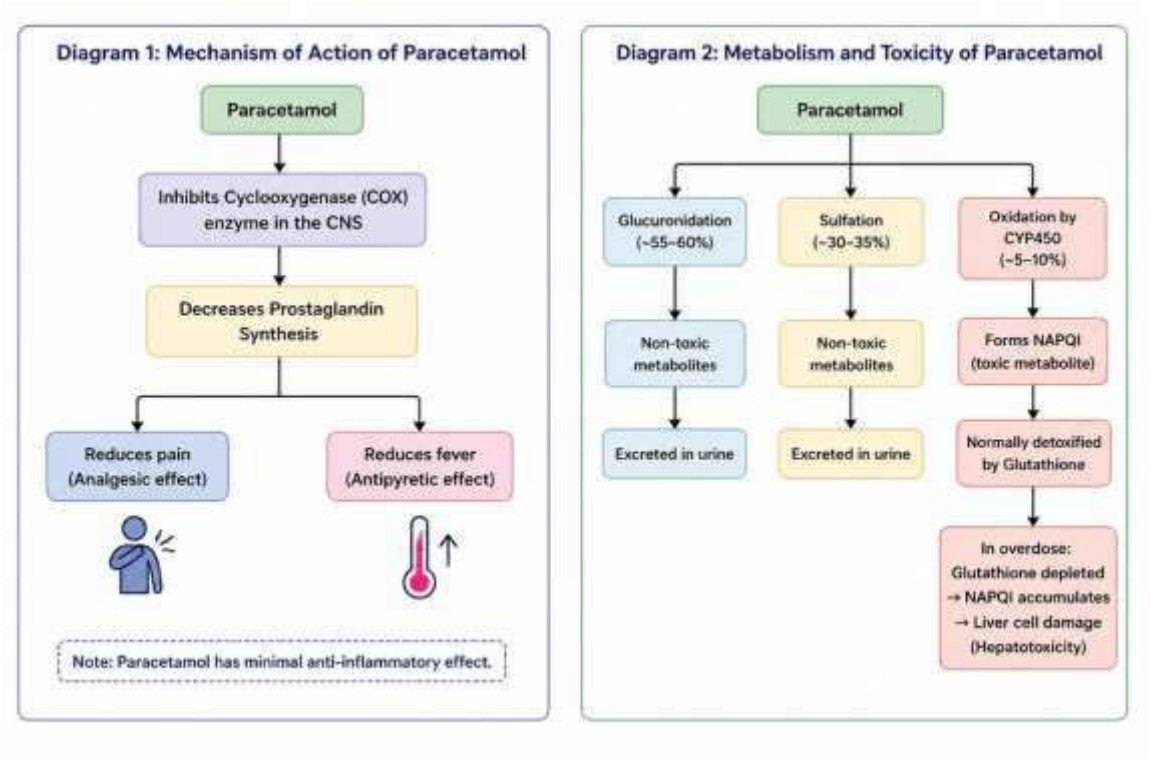

IV. THERAPEUTIC USES

The analgesic and antipyretic effects of paracetamol make it widely used in clinical practice. The effectiveness, safety, and availability of this drug make it a first-line treatment in the management of mild to moderate pain and fever. Treatment of fever caused by the infection of common cold, influenza, and other viral or bacterial diseases is one of the most common applications of paracetamol. It acts on the hypothalamic heat-regulating centre, and helps to reduce high body temperature, and to relieve symptoms. Another area of wide use of paracetamol is in the management of pain[29]. It can be used in the treatment of the mild to moderate pain such as headaches, toothaches, myalgia, back pain, joint pain. It is commonly used in dysmenorrhea (menstrual pain) and postoperative pain, either as a single agent or in combination with other analgesics. Paracetamol is a safer choice in patients in whom the use of the non-steroidal anti-inflammatory drugs (NSAIDs) is contraindicated- such as a patient with a gastric ulcer, bleeding disorder or hypersensitivity. It is also favoured in both pediatric and geriatric population because of the good safety profile when used properly. Also, paracetamol is often used in combination products with other drugs such as antihistamines, decongestants, and opioids to increase the therapeutic effect in such conditions as cold, cough, and severe pain. In general, the wide spectrum of therapeutic applications in combination with its safety and tolerability makes paracetamol one of the most fundamental and widely used drugs in the field of healthcare[30].

V. DOSAGE AND ADMINISTRATION

One of the most common drugs is paracetamol because it has well-established dosage requirements and its applicability across various age groups in administration. To ensure therapeutic efficacy and most importantly to reduce risk of toxicity, especially hepatotoxicity related to overdose, appropriate dosage and proper administration is essential.

Adult Dosage

The normal oral dose of paracetamol in adults is 500 to 1000 mg per 4 to 6 hourly as required by the patient in case of pain or fever. The highest amount of the drug that is recommended to be used per day is 4 grams (4000 mg). More commonly, however, particularly to promote safety, a lower maximal limit of 3-3.5 grams per day is frequently recommended. In people with impaired liver, chronic alcoholic use or malnutrition, dose changes might be needed since these conditions can predispose to toxicity. In these situations, it is advised to reduce dosing or increase dosing intervals[31].

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Paediatric Dosage

The dosing of paracetamol in children is calculated on the basis of body weight. The most commonly recommended dosage is 1015 mg/kg/day in 1 dose of 1015mg/kg/day every 46 hours. This is especially true in paediatric patients to prevent underdose and unintentional overdose. Paracetamol is usually found in paediatric preparations like syrups, suspensions, and suppositories, which make it easier to administer and adjust the dose based on weight[32].

Routes of Administration

There are various routes of administration of paracetamol, which offers flexibility in application to various clinical scenarios:

Oral Route: The most popular and the most convenient one. It is fast absorbing and can be used with the majority of patients.

Intravenous Route: This route is used in hospitals, particularly when the action needs to take place rapidly or when oral administration of the drug is impossible (e.g., postoperative patients, vomiting).

Rectal Route: The route is useful in paediatric patients or in situations where oral administration is not possible but absorption can be slower and unpredictable[33].

Special Populations

Elderly Patients: Generally safe but caution is necessary as there may be decreased liver functionality.

Pregnancy: It is relatively safe when taken in recommended doses under medical supervision.

Liver Disease: There is a need to reduce the dose to prevent build-up and toxicity.

Renal Impairment: It is usually safe, but in severe instances, dosing intervals might be required to alter[34].

Administration Considerations

Paracetamol can be taken with or without food, although food may slightly delay its absorption. To prevent overdosing patients should be advised to read labels carefully, particularly when using combination products so that they do not overdose themselves. The correct dosing schedule and the absence of several products containing paracetamol should also be taken into consideration. Healthcare workers, especially pharmacists, can contribute to patient education on how to use it safely, and how to avoid accidentally overdosing[35].

VI. CLINICAL STAGES OF PARACETAMOL

Stage	Time Period	Clinical Features
Stage 1	0–24 hours	Nausea, vomiting, sweating, fatigue, loss of appetite; sometimes asymptomatic
Stage 2	24–72 hours	Improvement of early symptoms, right upper abdominal pain, rise in AST and ALT
Stage 3	72–96 hours	Acute liver failure, jaundice, confusion, hypoglycaemia, bleeding, metabolic acidosis
Stage 4	>96 hours	Recovery of liver function or progression to multi-organ failure and death

6.1 Toxicity and Overdose: Paracetamol is considered to be mostly safe when it is used within recommended therapeutic doses, but an overdose is a severe medical condition that can cause severe liver damage and even death unless prompt attention is received. One of the most prevalent causes of acute liver failure all over the world is paracetamol toxicity, which has the highest prevalence due to its wide accessibility and use in various preparations[36].

6.2 Causes of Toxicity

The toxicity may be as a result of overdose whether intentional or unintentional. Intentional overdose has been linked with self-harm, whereas unintentional overdose might be caused by repeated high doses, use of multiple products containing paracetamol, or not being aware of the maximum dose per day. The possibility of toxicity is heightened by the fact that the total daily dose of more than 4 grams in adults increases the risk of toxicity. Doses that are higher than the recommended mg/kg limits may be harmful in children. Toxicity may also be caused by chronic excessive intake over a period of several days, even though the individual doses may not be very high. Some factors may make one more susceptible to toxicity, such as chronic alcoholism, malnutrition, liver diseases, and the use of drugs that cause liver enzymes. These circumstances increase the production of the toxic metabolite NAPQI, or decrease the capacity of the body to eliminate it[37].

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6.3 Pathophysiology of Toxicity

In normal conditions, paracetamol is mainly metabolized by the process of glucuronidation and sulfation to yield non-toxic metabolites. Only a small percentage is metabolized by the cytochrome P450 enzyme system resulting in the formation of NAPQI, a highly reactive intermediate[38]. NAPQI is conjugated with glutathione, a protective antioxidant found in liver cells, to quickly detoxify NAPQI in therapeutic doses. Nevertheless, during situations of overdose, the main metabolic routes are overloaded, and further acetamol is transformed into NAPQI. When glutathione stores are depleted, NAPQI starts to accumulate and binds to cellular proteins, which results in oxidative stress, dysfunction of mitochondria and finally hepatocellular necrosis. Most prominent in this damage is the liver, although in severe cases, damage to the kidneys and other organs may also be present.

6.4 Clinical Manifestations

The toxicity in the paracetamol follows a four-stage clinical progression with distinct clinical features:
Stage I (0–24 hours):
The symptoms tend to be mild and nonspecific with nausea, vomiting, sweating, fatigue and loss of appetite. It is possible that some patients will not exhibit any symptoms at this stage.
Stage II (24–72 hours):
The first symptoms can be improved, but the liver damage starts to appear. Patients can complain of pain in the right upper abdomen, and laboratory tests indicate an increase in liver enzymes (AST, ALT).
Stage III (72–96 hours):
This is the worst phase, and is marked by acute liver failure. Among the symptoms are jaundice, confusion (hepatic encephalopathy), hypoglycaemia, bleeding tendencies and metabolic acidosis. In extreme situations, this phase may be life-threatening.
Stage IV (>96 hours):
Patients slowly recover with a restoration of liver functions or go on to multi-organ failure and death[39].

6.5 Diagnosis

Paracetamol toxicity is diagnosed by patient history, clinical manifestations, and lab tests. Serum paracetamol levels are important to be measured, and it is interpreted with reference to the Rumack-Matthew nomogram, which helps to identify the risk of hepatotoxicity and make decisions regarding treatment. Tests of liver function (ALT, AST, bilirubin, prothrombin time) are necessary in order to measure the extent of liver damage[40].

6.6 Management and Treatment

Early management plays an important role in the prevention of severe liver injury. The main antidote to paracetamol poisoning is.
N-acetylcysteine (NAC). NAC works by:

- Replenishing glutathione stores
- Improving the paracetamol metabolism that is non-toxic.
- Directly neutralizing NAPQI

Most effective when taken within 8-10 hours of overdose but can still be effective even when given later.
The administration of NAC may be done orally or intravenously, according to the clinical circumstance. It is also necessary to provide supportive care, such as checking vital signs, fluid balance, and correction of metabolic abnormalities. Liver transplantation could be necessary in severe cases of liver failure[41].

6.7 Prevention of Toxicity

Prevention is important in curbing the occurrence of paracetamol toxicity. Key strategies include:

- Training patients on the maximum doses per day.
- The concomitant use of various products containing paracetamol should be avoided.
- Clearly labelling medications.
- Limitation of pack sizes in certain countries.

Pharmacists in particular can play a major role in maintaining safe use by counselling patients and offering the identification of potential risks[42].

Advantages

Paracetamol has some benefits that contribute to it being a highly favoured analgesic/antipyretic. When taken at therapeutic doses, it has a good safety profile, is effective in reducing pain and fever, and is effective in decreasing both the frequency and intensity of asthma attacks. In contrast to NSAIDs, it has the least gastrointestinal irritation and does

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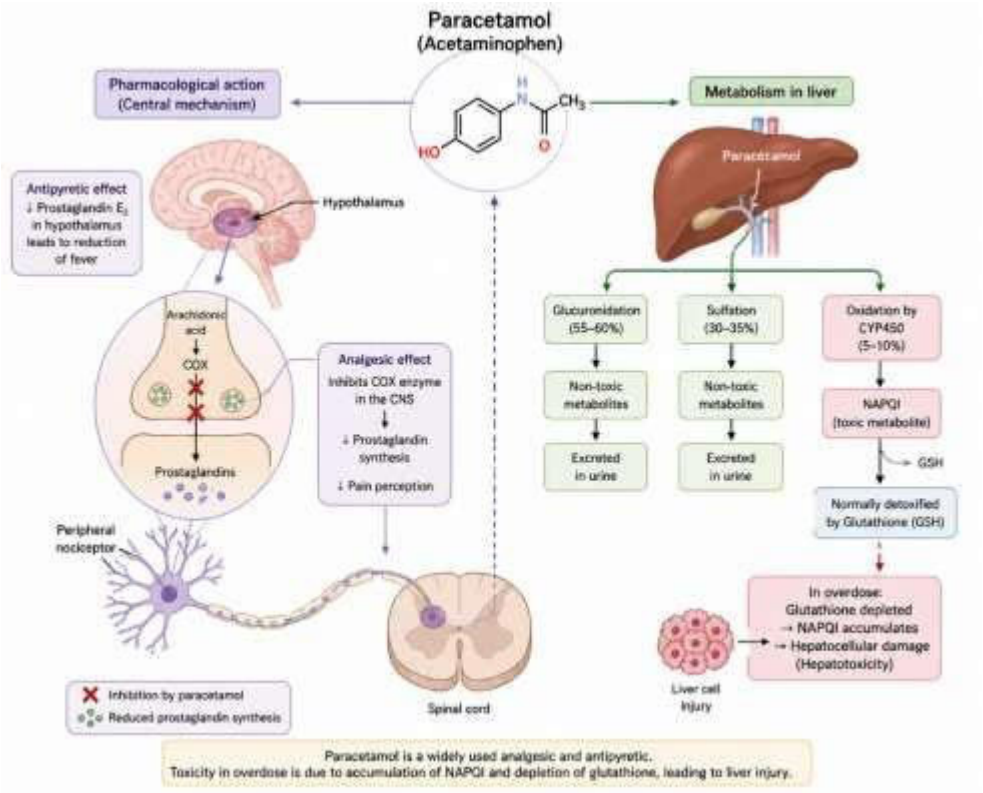
not produce any significant effect on platelet functioning or cause bleeding. It can be used as part of children, elderly patients, and pregnant women (under medical supervision). Also, its ease of access, affordability and various dosage forms make it convenient and accessible in clinical and home environments[43].



Limitations

Although Paracetamol has its advantages, it also has its limitations. It contains little or no anti-inflammatory action and hence it is not as useful in disorders where there is a lot of inflammation. The gravest restriction is the fact that in overdose, there is a risk of hepatotoxicity that can result in acute liver failure. Patients with liver disease, chronic alcohol use or malnutrition need caution. Also, unintentional overdose can be caused by its occurrence in several combination products. Therefore, careful dosing and patient awareness are essential for safe use[44].

VII. CONCLUSION

Paracetamol is so far one of the most common and vital drugs in terms of controlling pain and fever. Its efficacy, affordability, and desirable safety profile in therapeutic doses have made it a first-line option in clinical and community settings. This central mechanism of action of the drug coupled with minimal gastrointestinal and cardiovascular side effects is what makes the drug stand out in the market compared to other analgesics like non-steroidal anti-inflammatory drugs. Pharmacological characteristics of paracetamol, such as rapid absorption, predictable pharmacokinetics, and numerous administration routes, have led to its versatility and broad use in various patient groups. It is especially useful in patients in whom NSAIDs are contraindicated, like patients with gastrointestinal disorders or who are at risk of increased bleeding. Nevertheless, even with its benefits, paracetamol cannot be considered risk free. The presence of severe hepatotoxicity in the case of an overdose points to the importance of responsible use and the need to adhere to recommended dosing schedules. The development of toxic metabolites and the contribution of glutathione depletion to the necessity of creating awareness among healthcare professionals and patients. The early diagnosis and timely treatment with N-acetylcysteine have greatly enhanced the outcome in cases of toxicity.

However, prevention is the most efficient approach that encompasses the education of the patients, labelling, as well as close monitoring of drug use. To sum up, paracetamol remains a pillar in the treatment of pain and fever. Although it is normally safe and effective, its application should be informed by adequate knowledge and care to prevent any adverse

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effects. Its benefits can be maximized and the risks associated with its use can be minimized through rational use and increased awareness.

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