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Impact of Reality Extra Analgesic on Liver and Kidney Function in Male Rats

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الملخص— في هذه الدراسة، قمنا بتقييم تأثير دوا Reality Extra، وهو مسكن ألم شائع، مصنوع من الكافيين وديكلوفيناك الصوديوم والباراسيتامول، على فئران بيضاء حيث شُكِّلت مجموعتان من الفئران؛ تلقت إحداهما هذا الدواء لمدة 12 يومًا، بينما أُعطيت الأخرى محلولًا ملحيًا كمجموعة ضابطة. لتقييم آثار الدواء، فُحص عدد من المؤشرات البيولوجية والإنزيمية مثل مستويات اليوريا في الدم، ومستويات البيليروبين والكرياتينين في البلازما، وزيادة وزن الجسم، ووزن الكبد، ونشاط انزيمات الكبد AST و ALT في البلازما. أظهرت الفئران التي تلقت دواء Reality Extra مستويات أعلى بكثير لأنزيمات الكبد AST و ALT والكرياتينين، بالإضافة إلى انخفاض كبير في مستويات اليوريا مقارنةً بالمجموعة الضابطة. علاوة على ذلك، أظهرت الفئران التي تلقت دواء Reality Extra انخفاضًا غير ملحوظ في مستويات البيليروبين، وتشير هذه النتائج إلى أن دواء Reality Extra قد يؤثر سلبًا على وظائف الكلى والكبد مما يؤكد ضرورة إجراء المزيد من البحوث الدقيقة في مختلف البيئات السريرية.

الكلمات المفتاحية— باراسيتامول؛ كافيين؛ ديكلوفيناك؛ أسبارتات أمينوترانسفيراز

Abstract— In this study, we assessed how Reality Extra (RE), a popular analgesic composed of caffeine, diclofenac sodium, and paracetamol, affected in albino rats. Two groups of rats were formed; one group received Reality Extra for 12 days, while the other group was given saline as a control group. To evaluate the effects of the medication, a number of biological and enzymatic indicators were examined, such as blood urea levels, plasma bilirubin and creatinine levels, body weight gain, liver weight, and plasma aspartate aminotransferase (AST) and alanine transaminase (ALT) enzyme activities. Rats treated with Reality Extra had significantly higher levels of AST, ALT, and creatinine as well as significantly lower urea levels as compared to the control group. Furthermore, the rats given Reality Extra showed a non-significant drop in bilirubin levels. These results suggest that RE may negatively impact kidney and liver function, highlighting the need for more comprehensive research in diverse clinical contexts.

Keywords— Paracetamol; Caffein; Diclofenac; Aspartate aminotransferase

1. Introduction

Due to its effectiveness in reducing fever and pain in both adults and children, paracetamol is frequently administered in combination with caffeine [1]. This combination is a well-known mixed analgesic [2], that has been shown to be effective in treating tension-type headaches and migraines [3,4]. Several studies have reported that caffeine enhances the antinociceptive effects of

paracetamol in various pain conditions [5,6]. Early research suggested that caffeine and paracetamol may cause hepatotoxicity [7], which led to renewed interest in their toxicological effects in humans [8]. The focus remains on evaluating the hepatotoxic risks associated with this combination.

Recent studies have examined the various effects of diclofenac sodium, paracetamol, and caffeine on health. Animal studies have indicated that paracetamol, at lower doses, can elevate liver enzymes and induce apoptosis; at higher doses, it increases oxidative stress particularly in the brain [9]. In contrast, diclofenac has been linked to the deterioration of renal function by inducing oxidative stress [10]. These findings highlight the need for further research into the potential long-term adverse effects of these drugs. Hence, the objective of this study was to study the effect of Reality Extra, which is a combination of analgesic containing caffeine, diclofenac sodium, and paracetamol, on liver and kidney functions in male Wistar albino rats.

2. Materials and Method

2.1. Reality Extra (RE)

Reality Extra (RE), manufactured by Ratnatris Pharmaceuticals Pvt. Ltd., At-Indred, Kadi, Mehsana, Gujarat, India-342715, was used in this study. According to Table 1, each uncoated tablet contains anhydrous caffeine, diclofenac sodium, and paracetamol. For twelve days, each rat was given an oral dose of 7.23 g per 200 g of body weight in drinking water daily.

Table 1. Uncoated tablet constituents of Reality Extra

Item	Amount (mg)
Paracetamol BP	325mg
Diclofenac Sodium BP	50mg
Caffeine (Anhydrous) BP	40mg

2.2 Experimental Work

Ten fertile male Wistar albino rats weighing approximately 190 g were obtained from the animal house of the Zoology Department at Derna University, Libya, and used for the experimental design. Free access to a standard diet comprising 21.27% protein, 2.83% fat, and 2.46% fiber was provided. Water was allowed ad libitum. They were kept in well-ventilated conditions with a 12-hour light/dark cycle. The rats (n = 10) were divided into two groups (n = 5 each): the Reality Extra-treated group (RE), which received a standard meal with the drug, and the control group (C), which was fed a standard diet only. Body weight was monitored daily for 12 days during the treatment period. For both the control and RE groups, the percentage of total body weight gain was recorded. At the end of the treatment period, the animals were slaughtered and dissected; blood was collected via cardiac puncture, and the liver was extracted and weighed. Biochemical evaluations of kidney and liver function were then performed and analyzed.

2.3 Biochemical Investigation

As directed by the Biolabo Assay Kit Manual (Cat# 80027), the levels of plasma aspartate aminotransferase (AST) and alanine transaminase (ALT) were measured. In accordance with the guidelines provided in the Agappe Assay Kit Manual (Cat# 51003005), plasma bilirubin levels

were measured. As directed in the Biomaghreb Assay Kit Manual (Cat# 25043), plasma creatinine levels were measured. Blood urea nitrogen (BUN) and plasma urea levels were measured in accordance with the guidelines provided in the Biolabo Assay Kit Manual (Cat# 92032).

2.4 Statistical Analysis

To compare the various values, statistical analysis was done between the experimental and control groups. Results were expressed as means ± SE. Statistical significance was calculated using one- way analysis of variance (ANOVA) followed by post hoc tests for multiples comparisons. All the statistical analysis was carried out with the use of SPSS 23 software. Differences were considered significant at $P \leq 0.05$.

3. Results

3.1 Body Weight and Liver Weights (Absolute and Relative)

According to Table 2, the percentage of body weight gain in male rats given Reality Extra for 12 days was significantly lower (5.61±2.50) than in the control group (23.38±2.59). Table 2 also presented the values of F-test which is a statistical test used to determine if there are significant differences between the means of two groups. Male rats given reality extra for 12 days showed a noticeable but non-significant rise in both absolute and relative liver weight when compared to the control group as shown in Figure 1. Each result indicates the mean ± SE (n=5) and significant at $P < 0.05$ is indicated by a *. Abbreviations: RE, Reality Extra; C, control.

Table 2. Percentage increase in body weight of male rats treated with Reality Extra for 12 Days

Body weight of male rats	C	RE	F test
Starting body weight	167.6±4.20	219.2±18.47	7.47
Body weight after 12 days	218.20±5.65	235.20±22.81	0.52
Increase percentage in body weight	23.38±2.59	5.61±2.50*	24.61

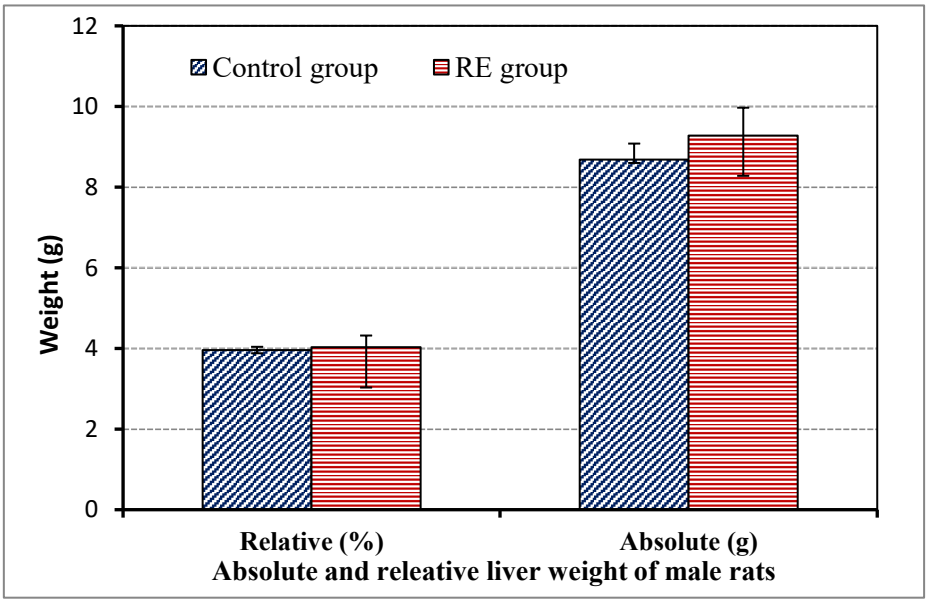

Figure 1. The male rats' absolute and relative liver weight after receiving Reality Extra for 12 days. The mean ± SE is represented by each result (n=5). Significant at P<0.05 is indicated by a *. C stands for Control, and RE for Reality Extra.

3.2 Biochemical Observations

When comparing the RE-treated group to the control group, there was a considerable increase in AST and ALT activity as shown in Figure 2**.** According to Figure 3**,** male rats given reality extra showed a noticeable but non-significant decrease in plasma bilirubin levels compared to the control group. In contrast, plasma creatinine levels were significantly elevated in the RE-treated group compared to the control group. Compared to the control group (49.60 ± 3.15 and 23.17 ± 1.47, respectively), plasma urea and blood urea nitrogen (BUN) levels were significantly lower in the RE group (32 ± 2.12 and 14.90 ± 0.98, respectively), as indicated in Figure 4.

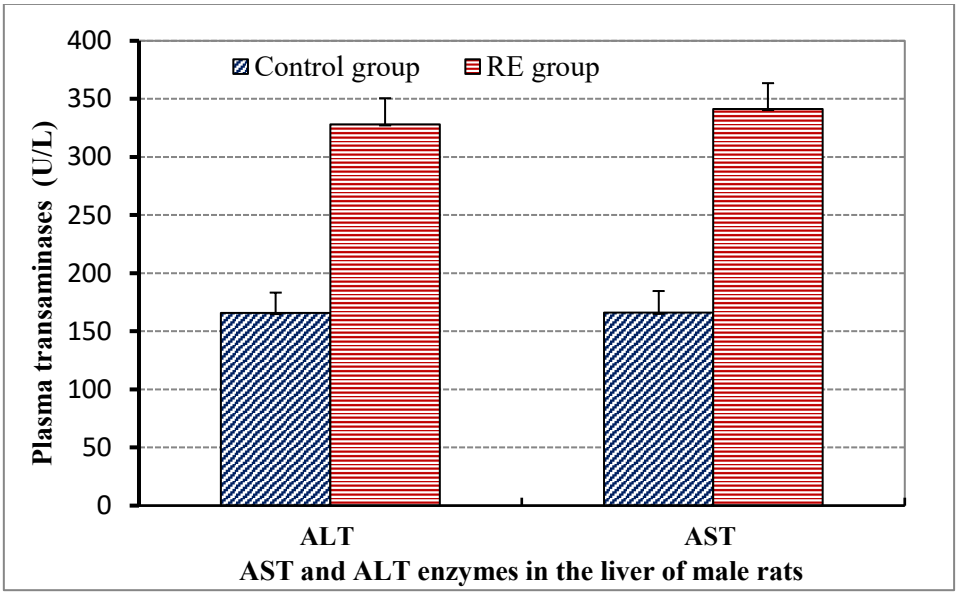

Figure 2. The amounts of plasma transaminases in male rats given Reality Extra for 12 days. The mean ± SE is represented by each result (n = 5). Significant at $P < 0.05$ is indicated by a *. C stands for Control, and RE for Reality Extra

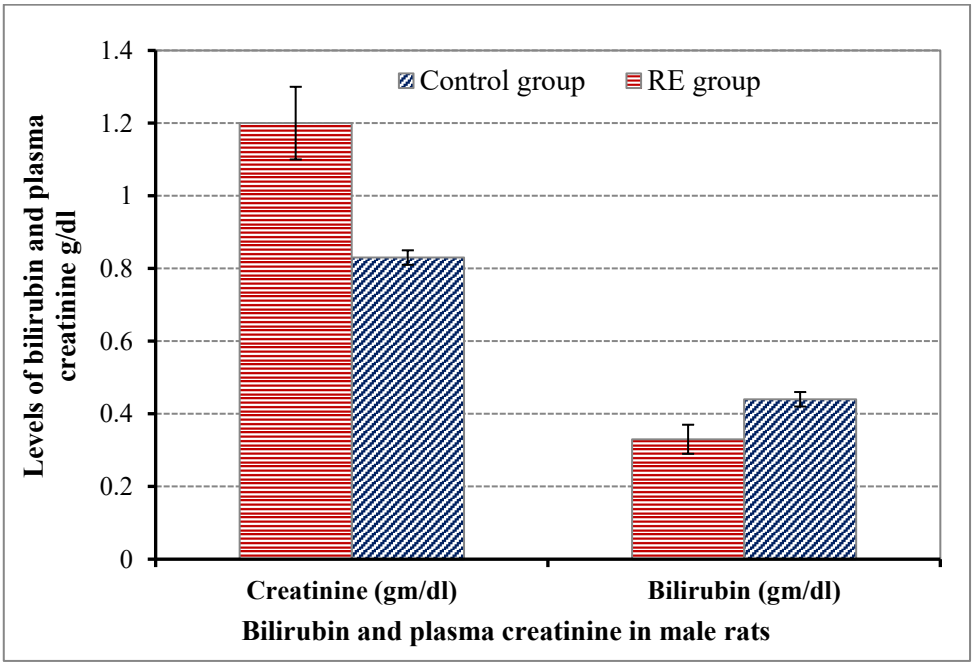

Figure 3. The levels of bilirubin and plasma creatinine in male rats given Reality Extra for 12 days. The mean ± SE is represented by each result (n = 5). Significant at $P < 0.05$ is indicated by a *, C stands for Control, and RE for Reality Extra

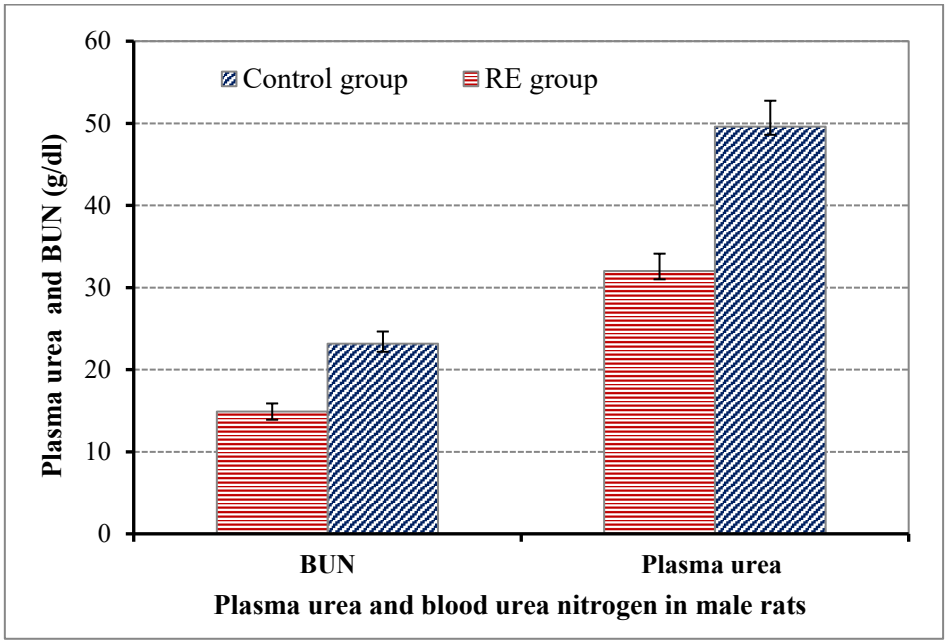

Figure 4. Plasma urea and blood urea nitrogen levels of male rats treated Reality Extra for 12 days. Each result represents the mean ± SE (n = 5). Significant at $P < 0.05$ is indicated by a *, C stands for Control, RE for Reality Extra, and BUN for blood urea nitrogen

4. Discussion

According to our findings, the percentage of body weight gain in male rats treated with Reality Extra for 12 days was significantly lower (5.61 ± 2.50) than in the control group (23.38 ± 2.59). This result implies that Reality Extra might significantly affect appetite regulation or metabolic functions. The toxicity and therapeutic effects of diclofenac, caffeine, and paracetamol were the main topics of earlier research, although weight changes were not specifically covered. However, it is important to note that paracetamol has been widely used due to its lower gastrointestinal adverse effects compared to Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), which may indirectly impact body weight through changes in appetite or metabolism [11].

The results also revealed that, male rats given Reality Extra showed a non-significant increase in liver weight, both in absolute and relative terms. AST and ALT levels, however, increased significantly, suggesting possible liver injury or stress. Similar hepatic stress may be induced by Reality Extra, as research has demonstrated that diclofenac administration can raise liver enzymes and result in severe liver deterioration [10].

In contrast to earlier findings where paracetamol administration led to elevated bilirubin levels due to liver damage, our study demonstrated a non-significant decrease in plasma bilirubin levels in male rats treated with Reality Extra [12]. This disparity may result from Reality Extra's distinct composition, which may contain substances that provide some hepatoprotection similar to the hepatoprotective effects of nitroparacetamol [13].

Moreover, plasma creatinine levels of the reality extra group were noticeably higher (Fig. 3), suggesting possible renal damage. This outcome is in line with the research reported by Peng et al. [12], who found that paracetamol intoxication caused severe kidney damage, including acute renal failure and renal tubular injury. Furthermore, it has been demonstrated that diclofenac damages

kidney function through oxidative stress pathways, which raise renal indicators including urea and creatinine [10].

The blood urea nitrogen and plasma urea levels of reality extra group were significantly decreased compared to the control group. This observation contrasts with typical indicators of renal impairment, which often show elevated urea levels along with elevated creatinine levels. The components of Reality Extra might interact in a complex way, affecting renal function in an unpredictable manner. Although diclofenac and paracetamol have been shown in earlier studies to alter renal parameters, the effects can vary depending on dosage and chemical interactions [14].

Overall, the results of current study demonstrate notable physiological alterations linked to Reality Extra treatment, especially in indicators of renal function and liver enzyme activity. These findings suggest unique or synergistic effects due to the specific formulation of Reality Extra, although they generally align with the existing body of research on the hepatotoxic and nephrotoxic effects of paracetamol and diclofenac. Further research is needed to clarify the precise mechanisms and potential protective factors against these adverse effects.

Eventually, the findings of the study suggest that patients taking Reality Extra–a combination medication containing caffeine, diclofenac sodium, and paracetamol should have their liver enzymes and renal function monitored regularly**.** To minimize the risk of toxicity, healthcare providers should exercise caution when prescribing Reality Extra, especially to patients with pre-existing liver or kidney conditions. Alternative treatments or dosage adjustments should also be considered.

5. Conclusion

This study demonstrated that Reality Extra, which is a combination of analgesic containing caffeine, diclofenac sodium, and paracetamol, significantly affects both liver and kidney functions in male Wistar albino rats. The treatment group showed elevated plasma levels of AST, ALT, and creatinine, indicating potential hepatic and renal damage. Furthermore, a significant reduction in body weight gain and urea levels was observed, suggesting an impact on metabolic activity and kidney function. These findings highlight the toxicological risks associated with the prolonged or unmonitored use of Reality Extra. Therefore, it is recommended that patients receiving this drug undergo regular monitoring of liver and kidney function, particularly those with pre-existing hepatic or renal conditions. Clinicians should carefully weigh the risks and benefits when prescribing Reality Extra and consider alternative treatments or dose adjustments where necessary. Further studies are needed to investigate the long-term effects, underlying mechanisms of toxicity, and possible protective strategies in both animal models and human clinical settings.

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