ASSESSMENT OF THE PATHOLOGICAL AND PHYSIOLOGICAL EFFECTS OF HESPERIDIN ON RENAL DAMAGE IN RATS INDUCED BY GENTAMICIN

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ABSTRACT

This research was conducted to establish the renal protective effect of the 100 mg/kg body weight (B.W) hesperidin (HES) against 100 mg/kg mediated nephrotoxicity of gentamicin (GNT) in rats. For the treatment of Gram-negative bacterial infections, GNT is used. Because of nephrotoxicity, however, GNT administration is restricted. Twenty male rats were divided evenly into four groups: group (1) control (1 ml/kg saline orally), group (2) GNT (100 mg/kg), intraperitoneal (i/p)) and group (3) HES (100 mg/kg) and group (4) GNT (i/p) plus HES were administered orally for (14) consecutive days. For consecutive (14) days. On the (15) day of experimentation, all the rats were killed, and then blood and kidney samples were taken. A substantial (p<0.01) decrease in body weight, and a significant (p<0.01) rise in Serum creatinine (CR), Blood urea nitrogen (BUN), Urea (UR), Malonaldehyde enzyme (MAD) and histopathological improvements in group 2 have demonstrated GNT-induced nephrotoxicity. Protective effect of renal toxicity and GNT-induced oxidative damage by substantially improving (p<0.01) by raising body weight and decreasing CR, BUN, UR, MAD and improving HES tissue morphology (100 mg/kg) (group 3,4). These discoveries ensure that HES (100 mg/kg) cell reinforcement impacts will secure GNT-instigated nephrotoxicity in rats.

Key words: Hesperidin , Gentamicin , Anti-oxidant , Rats.

1. INTRODUCTION

Antibiotics are one of the most commonly used groups of medicines. Many complications caused by infections avoid these medicines. Antibiotics have side effects and can affect the liver, kidney, brain, blood, skin and eyes of different body organs, including (1). Aminoglycoside anti-toxins, particularly GNT, are generally used to treat genuine Gram-negative microbes contaminations. (2) . Kidney injury, which is one of the critical reasons for kidney failure in an enormous number of individuals taking this medication, are the primary results. In this manner, consuming these medications faces downsides because of the way that nephrotoxicity is one of the principle results of Gentamicin. (3,4) . GNT-prompted nephrotoxicity has been recorded in research facility creatures (5). GNT increments oxidative pressure and free extreme creation and hinders the cancer prevention agent safeguard component in the kidney. This decreases non-enzymatic and enzymatic cell reinforcements, adding to the over-creation of responsive oxygen species (ROS). This can upset the lipids, proteins and nucleic acids of the layer, adding to renal poisonousness, brokenness and injury. (6). Flavonoids are a gathering of mixtures that happen normally and are unequivocally present in food varieties of plant beginning. In different mammalian cell frameworks, in vitro just as in vivo, flavonoids have various natural impacts. Mitigating, subterranean insect hypersensitive, antiviral, antibacterial, and antitumor action have been appeared to exert7). The pharmacological consequences for specific proteins, just as their cell reinforcement movement, hinder their ability. (8) Hesperidin is a glycoside of flavone got from "hesperidium," the sort of organic product that citrus trees develop as it is plentifully present in citrus natural products. (9) Hesperidin is principally utilized as a cell reinforcement since oxidative pressure markers like receptive oxygen species (ROS) and lipid peroxidation levels have only sometimes been forestalled in a portion subordinate manner.(10) Hesperidin might be related with possible benefits, like diminished narrow porousness, mitigating, antimicrobial and insect cancer-causing impacts, in the anticipation of a few sicknesses. Hesperidin additionally controls the amalgamation of hepatic cholesterol by constraining the movement of the reductive 3-hydroxy-3-methylglutaryl coenzyme A(HMG-CoA) (11-14(. Likewise, in diabetic
hares, it is distinguished as an antihyperlipidemic,(15) antihypertensive,(16) and cardioprotective action in ischaemic coronary illness. (17).

II. MATERIALS AND METHODS

In April 2019, this thesis was carried out in the pathology department of veterinary medicine at AL-Qassim Green University/ Iraq.

Drugs

Hesperidin (HES), 100% safe, was purchased from BULK Supplements.com USA. KEPRO-HOLLAND purchased Gentamicin (GENT), Gentject 10%. Ketamine: 10% inj. BY KEPRO-HOLLAND. Xylazine, XYL-M2 and VMD-Belgium, respectively.

Rats experimental:

In this study, twenty healthy male rats weighing 154-157 g and aged (120-200) day were included in the number of laboratory animals used in the experiment, obtained from the animal house of the College of Veterinary Medicine, Baghdad University, before the beginning of the experiment, held for 15 days as an acclimatization period. The animals were preserved and fed a regular pellet diet and water under standard housing conditions. Twenty rats were randomly divided into four equal groups after a quarantine duration of 15 days, each group consisting of 5 rabbits, and GENT was injected intraperitoneally (i/p) at a dose of (100 mg/kg/day) for (14) consecutive days. GENT dose was chosen according to previous studies showing major renal toxicity (18,19) and was treated.

Weight of body

The automated electronic balance was used to weigh all animals before and after treatment.

III. PREPARING SERUM

Rats were fasted for (10) hours at the end of the experimental duration, anesthetized with ketamine (75 mg/kg) combined with xylazine (2.5 mg/kg). In non-heparinized tubes, blood samples were obtained by heart puncture, centrifuged at (4000) rpm for 10 minutes. The samples were used to test (CR), (BUN), (SU) and (MDA) concentration levels after extracting the serum from the clot using a sampler and histopathological tests were performed. About Bancroft, et al (23).

Analysis of statistics

The statistical analysis, according to Al-Zubaidy and Al-Falahy, was carried out using the Full Randomized Design (CRD) method (24). The mean differences between the averages of the characteristics tested were calculated using the Duncan test at the likelihood level of (0.01) (25). The statistical data was analyzed using the (SAS 2010) (26).

Results:

Weight of body

In the groups of rats given GNT either alone or in combination with HES, I/P injection of GNT, no deaths were observed, generating a substantial (P<0.01) decrease in body weight compared to control. Before and after the experiment, the animals were weighed, while HES care was considered. Important (P<0.01) increase in body weight (100 mg/kg) relative to GENT control rats (Table 1).

HES Impact. Alterations to renal function parameters caused by GENT

The effect of GENT caused a decrease in rat kidney function. After (14) days of treatment with GENT, a significant (p ?? 0.01) increase in serum (CR), (BUN),(UR) levels compared to the control group and a significant (p < 0.01) increase in (MDA) levels compared to the control was observed. Whereas, HES treatment. GENT prevented (100 mg/kg) induced serum (CR) (BUN) (UR) increases (p < 0.01) and produced a substantial (P < 0.01) decrease in (MDA) relative to GENT control rats. Nevertheless, HES. (100 mg/kg) has a strong body weight effect as compared to GENT control rats, serum' (table 2).
Table 1: Impact on initial and final body weight (mean ± SE) of HESP and GENT use.

<table>
<thead>
<tr>
<th>Traits</th>
<th>Control Mean ± SE</th>
<th>Gentamicin Mean ± SE</th>
<th>Hesperidin Mean ± SE</th>
<th>Gentamicin + Hesperidin Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight at 1 day (g/animal)</td>
<td>157.366 ± 3.26 A</td>
<td>155.870 ± 1.76 A</td>
<td>154.350 ± 1.85 A</td>
<td>157.038 ± 0.72 A</td>
</tr>
<tr>
<td>Weight at 14 day (g/animal)</td>
<td>162.350 ± 1.58 A</td>
<td>136.332 ± 1.79 D</td>
<td>160.178 ± 1.60 B</td>
<td>160.352 ± 2.02 C</td>
</tr>
</tbody>
</table>

The vertically distinct letters that relate to major differences at 0.05 or 0.01.

Table 2: HES Impact. Shift in renal function in rats due to Gentamicin-induced

<table>
<thead>
<tr>
<th>Traits</th>
<th>Control Mean ± SE</th>
<th>Gentamicin Mean ± SE</th>
<th>HES Mean ± SE</th>
<th>Gentamicin+ HES.100mg/kg Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.640 ± 0.02 C</td>
<td>3.224 ± 0.23 A</td>
<td>0.822 ± 0.03 B</td>
<td>1.170 ± 0.05 B</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>25.132 ± 0.11 C</td>
<td>49.890 ± 0.33 A</td>
<td>22.582± 0.34 C</td>
<td>37.846 ± 0.63 B</td>
</tr>
<tr>
<td>Serum urea (mg/dl)</td>
<td>63.658 ± 0.72 C</td>
<td>68.646 ± 0.60 A</td>
<td>64.076 ± 0.70 C</td>
<td>67.368 ± 0.71 B</td>
</tr>
<tr>
<td>Malonaldehyde (Mole/L).</td>
<td>0.562 ± 0.09 C</td>
<td>3.940 ± 0.05 A</td>
<td>0.890 ± 0.03 C</td>
<td>2.424 ± 0.12 B</td>
</tr>
</tbody>
</table>

Horizontally, the various letters which relate to significant differences at 0.05 or 0.01.

**HES Impact. Histopathologic alteration in renal tissue caused by GENT**

Histopathological analysis the light microscopic examination of the kidney using H&E (400X) stain in control rats showed a typical histological structure of the tissue of the kidney (Fig. a). Histopathological effects of GENT on the kidneys of treated rats include maculation of glomerular tuft mesangial cells with coagulate necrosis in some renal tubules infected with inflammatory cells (Fig. b). Interstial mononuclear cell infiltration In rabbits treated with HESP for 21 days, histopathological effects of HESP on the kidney of treated rats have been reported., (Fig. c). Histopathological effects of the GENT mixture. Rats are presented with plus HESP on the kidneys of treated rats. Treated with HESP plus CIPR for 21 days, large and circular proliferation of glomeruli with regeneration of tubular basophils in renal convoluted tubules was observed (Fig. d).
The body weight saw in Table 1 demonstrates that a considerable diminishing in the body weight of G2 comparative with G1, G3 and G4 was seen at 100 mg/kg.b.w. Expanded catabolism and anorexia may prompt diminished food admission and further declines in body weight after loss of cylindrical cells, inclusion in renal water reabsorption prompts parchedness and body weight reduction (27). This weight reduction can be expected either to guide harm to renal tubules bringing about water reabsorption powerlessness of the rounded cells, prompting lack of hydration and body weight loss (28) or to expanded catabolism bringing about acidosis, anorexia and diminished food admission (29). GENT is an aminoglycoside anti-toxin, its restorative use is restricted by nephrotoxicity as a result of all aminoglycosides, particularly GENT (30). The result of this investigation showed that GENT creates nephrotoxicity at a portion of (100 mg/kg/day) and is described by a reduction in renal capacity since it was related with a huge expansion in serum (CR), (BUN) and (UR) levels., There is a diminishing in the limit of the kidney to channel (CR), (BUN) and (UR) levels due to limited glomerular filtration rate or glomerular harm, hyproduct is delivered in pee (31, 32). Significant changes in renal (MDA) levels were found in GENT rodents comparative with control rodents, with oxidative pressure being the primary driver of GENT interceded renal harm in the flow research. This view is affirmed by a significant ascent in degrees of lipid peroxidation (MDA) since the expansion in TBARS, which is the final result of lipid peroxidation, was likewise demonstrated to be comparable in different investigations (33,34). These (CR)-, (BUN)-, (UR) and (MDA) levels have diminished fundamentally with HES. Treatment with (100 mg/kg). The Malonaldehyde enzyme increase observed in Table 2 indicates that there was a substantial increase in G2 relative to G1, G3 and G4 at 100mg/kg.b.w. It could be due to the GENT administration. These findings are in accordance with those obtained by other investigators caused by elevated levels of Malonaldehyed (35). Malonaldehyed is a stable free radical-mediated lipid oxidation cascade metabolite and is
commonly used as a stress marker that causes oxidation and lipid destruction (36). Lipid oxidation is an important cause of cell membrane degradation and is believed to be involved in the creation of tissue injury (37).

Renal severe necrosis and penetration into several glomeruli, atrophy of glomeruli, moderate bleeding in renal tissue and natural proliferation of epithelial cell line tubules have been reduced by histopathological changes caused by GENT, and renal tubules are regenerated in HESP at the dose (100 mg/kg, g.b.w.) of treated rats. Our findings indicate that the ameliorative effect of hesperidin (100 mg/kg, g.b.w.) on GENT causes kidney toxicity in rats for a duration of 14 days. HESP is a safe and pharmaceutically active bioflavonoid with antioxidant and free radical scavenging properties contained in citrus fruits (38). HESP's ability to scavenge free-radicals has resulted in oxidative stress that adversely affects the structure and function of cells. Oxidative stress induces inflammation, which, in a vicious circle, further potentiates oxidative stress. Triggering numerous diseases that endanger life, ranging from cardiovascular and neurodegenerative diseases and cancer(39). Not only does HESP scavenge ROS, but it can activate endogenous anti-oxidant resistance mechanisms as well. HESP offers invaluable support for oxidative stress-related disorders and provides protection against stress that causes radiation therapy and chemotherapy care (40). The active component responsible for increasing the secretion of ghrelin is HESP. Ghrelin is also referred to as a hunger hormone that enhances appetite, secretion of gastric acid and gastric motility (41). HESP also serves as an anti-bacterial, antifungal and anti-viral infection (42). This can be explained by the effects of HESP on anti-inflammatory, anti-oxidant and antimicrobial activity in protecting cells from damage such as free-radicals from oxidative stress caused by GENT, HESP can be used at a dosage (100 mg/kg, bw) administration showed a marked renal protective activity. The protective effects of HESP (100 mg/kg, bw) may be synergistic or individually triggered by its anti-oxidant or anti-inflammatory effects with anti-bacterial activity.

V. CONCLUSION

The GENT government. By inhibiting free-radical development and restoring anti-oxidant protection mechanisms, HESP at a dose (100 mg/kg, bw) prevents renal dysfunction. Thus, administration has contributed to a decline in the side effects of GENT use alone.

Conflict of Interest

Nil

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REFERENCES


