In-vivo Evaluation of Natural Products Against Nephrotoxicity Caused by Acetaminophen

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ABSTRACT

Acetaminophen or AAP is a widely used antipyretic-analgesic drug that causes nephrotoxicity at higher than the effective doses. The aim of this study is used to determine the nephroprotective effect of brown seaweed, *Jolyna laminarioides* (*J. laminarioides*) against AAP toxicity in rats by checking their biochemical parameters, via using their kidney parameters, electrolytes, lipid parameters, and glucose were estimated to find nephrotoxicity. Furthermore, lipid peroxidation: malondialdehyde (MDA), anti-oxidative markers: reduced glutathione (GSH) and catalase, expression of inducible nitric oxide synthase (iNOS), and histological examination were also performed to determine the changes in kidney architecture. Our results showed that the AAP raised the kidney markers and decreased GSH and catalase activity while raising MDA level, iNOS and showed injuries in histopathological examination of the kidney when compared with normal control groups. In AAP-treated rats, ethanol extract of *J. laminarioides* decreased the raised levels of renal parameters along with glucose and lipid profile. It also showed protection in antioxidant, inflammatory markers and effectively improved the cellular architecture of the kidney. The findings of this study provide evidence of *J. laminarioides* which possesses a nephroprotective effect and can attenuate AAP which causes renal dysfunction and can be mediated not only by its well-known biochemical parameters but also by its antioxidant and anti-inflammatory activity.

Keywords: Acetaminophen, J. laminarioides, Nephrotoxicity, Seaweed

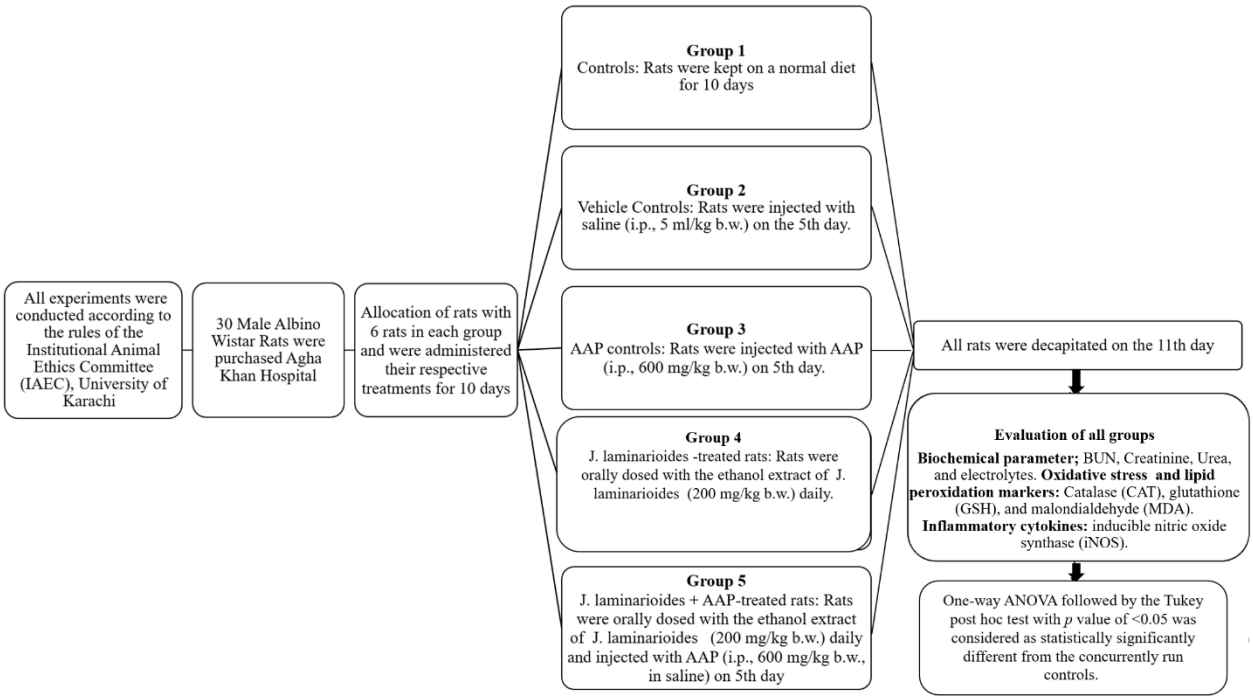
INTRODUCTION

The most commonly used drug is AAP which is an antipyretic-analgesics drug around the world. This drug helps with mild to moderate headaches, postpartum pain, and muscle aches [1]. AAP can be used as an analgesic adjunct to anti-inflammatory therapy and although it can be used as an inadequate therapy for treating inflammatory diseases such as rheumatoid arthritis [2]. In general, AAP is thought to cause acute renal failure in 1-2% of patients [3]. N-Acetyl-p-benzoquinone (NAPQI) is present in the microsomal P_{450} enzyme system and oxidizes most of the AAP taken up by therapeutic doses of GSH (intracellular glutathione) [4]. The main symptom of AAP toxicity is acute necrosis in renal tubules by examining levels of renal parameters (urea and creatinine) [5]. In any organism, if the drug toxicity is raised it generates free radicals and oxidative stress has a profound effect on AAP, leading to severe liver injury and progressive renal failure. Nature has been considered as a source of medicinal products for decades, and certain valuable medicines have been developed from a wide range of plant sources. In marine algae, seaweed has been used as medicine because of its health benefits. Marine algae are known as a valuable source of bioactive compounds, polysaccharides, phytochemicals, vitamins, and minerals such as sodium, phosphorus, calcium, and potassium [6]. Several studies are available regarding AAP-induced hepatotoxicity and its mechanisms but only some studies have reported that AAP-induced nephrotoxicity [5].

OBJECTIVES

The aim of this study is to determine the protective role of *J. laminarioides* against AAP-induced renal dysfunction.

METHODOLOGY



RESULTS / CONCLUSION

Our results showed that AAP increased renal markers; creatinine (150%), urea (161.1%), and BUN (160.2%) indicated renal damage, while electrolyte levels decreased; K^+ (−6.8%) and Ca^{++} (− 12.5%) as compared to normal control. In addition, AAP-poisoned rats also showed significant increases in lipid profiles (Total cholesterol and Triglycerides) and glucose up to (229% & 148%) and (82.9%) as compared to normal control groups. In AAP-treated rats, ethanol extract of *J. laminarioides* significantly (p<0.05) reduced renal parameters and increased Mg^{++} (11.1%) and K^+ (9.7%) levels as compared to AAP control rats. Besides these, ethanol extract of *J. laminarioides* in AAP-treated rats also showed significantly (p<0.05) decreased lipid profile; [total cholesterol (−24.6) and triglycerides (−8.3%)] and glucose (−22.3%) compared to AAP control.

The activity of selected antioxidant enzymes; [GSH and catalase] and lipid peroxidation (MDA) in kidney tissues were also examined. A single dose of AAP caused a decrease in catalase activity (-50%) and GSH levels (-28%) while MDA level up to (64.7%) compared to normal control rats. An ethanol extract of *J. laminarioides* in AAP-treated rats showed a slight raise in catalase activity (25%), restored the decreased GSH levels (9.7%), and significantly (p<0.05) decreased MDA (−18.6%) in the kidney as compared to the AAP control group.

The histological structure of the AAP-treated group compared with the normal control group is characterized by damaged glomerulus (GL) with endothelial rupture of Bowman's capsule (BM) and degenerated tubules with severe tubular dilatation in renal tissue. These changes were diminished in AAP-dosed rats fed with an extract of *J. laminarioides* by showing the normal architecture of GL and showed no tubular degeneration, which indicated the normal structure of the GL and significant renal protection.

In kidney tissue, iNOS gene expression showed higher iNOS levels in the AAP control group compared to the

normal control group. However, ethanol extract of *J. laminarioides* in AAP-treated rats decreased mRNA expression of iNOS.

Therefore, we conclude that in this era of technology and science, the demand for remedies from natural products is growing day by day due to their curative efficacy and lack of side effects. As the current finding revealed that *J. laminarioides* is a promising seaweed for the development of phytomedicine against their ailments and requires further research in this direction.

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REFERENCES

1. Altabakhi, Ibrahim W., et al. "Acetaminophen/Aspirin/Caffeine." StatPearls [Internet]. StatPearls Publishing, (2021).
2. Fokunang, Charles, et al. "Overview of non-steroidal anti-inflammatory drugs (NSAIDs) in resource limited countries." Moj Toxicol 4.1 (2018): 5-13.
3. Hiragi, Shusuke, et al. "Acetaminophen administration and the risk of acute kidney injury: a self-controlled case series study." Clinical Epidemiology 10 (2018): 265-276.
4. Athersuch, Toby J., et al. "Paracetamol metabolism, hepatotoxicity, biomarkers and therapeutic interventions: a perspective." Toxicology research 7.3 (2018): 347-357.
5. Sohail, Nida, et al. "Marine macro-algae attenuate nephrotoxicity and hepatotoxicity induced by cisplatin and acetaminophen in rats." Environmental Science and Pollution Research 26.24 (2019): 25301-25311.
6. Sohail, Nida, et al. "Nephroprotective effect of ethanol extract and fractions of a sea lettuce, Ulva fasciata against cisplatin-induced kidney injury in rats." Environmental Science and Pollution Research 28.8 (2021): 9448-9461.