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Orignal Article

The Effect of Methanolic Extract of Corn Silk in Gentamicin Induced Acute Renal Injury in Rats Model

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ABSTRACT

Corn Silk is a worthwhile herb that possesses health-promoting nutrients including flavonoids. The bioactive compounds in Corn Silk that are beneficial for health include vitamins, carbohydrates, magnesium, proteins, calcium, sodium and magnesium salts, alkaloids, steroids, and volatile salts, potassium, flavonoids, and many other phenolic compounds. Maysin is one of the flavonoids in Corn Silk. The present study highlights the therapeutic effects of Corn Silk in Acute Renal Injury (ARI). **Objective:** To observe the effect of methanol extract of corn silk on Gentamicin induced ARI. **Methods:** An experimental study was conducted. A total of18 rats were divided into 3 groups each containing 6 rats. ARI was induced in all 18 rats by injecting Gentamicin (100mg/kg/BW) intra-peritoneal for 7 days. After the induction of ARI (Serum Urea ≥ 10-50 mg/dl, Creatinine ≥ 0.5-1.4), the treatment was started. The first group (G0) received isotonic saline (0.1ml/kg/BW), 2nd group (G1) received Corn Silk extract (200mg/kg/BW) orally, and 3rd group (G2) received Corn Silk extract (300mg/kg/BW) orally. This treatment was given to rats for 21 days. During this study body weight of each rat was also measured. The assessment of different biochemical parameters such as Serum Urea and Creatinine level was done. **Results:** The results showed that corn silk extract helped in the treatment of ARI by reducing the elevated renal parameters. Moreover, a reduction in weight was also observed. **Conclusions:** Corn Silk extract has significantly reduced Serum Urea and Serum Creatinine levels. The present study highlights the therapeutic potential of Corn Silk in ARI induced by Gentamicin in rat models.

INTRODUCTION

Acute renal Injury (ARI) is a sudden loss of renal functions and the ability to eliminate extra fluids and waste materials from the blood. ARI has a high rate of mortality and is a life alarming disease. Oxidative stress and inflammation are the most important mechanisms of ARI. Shortness of breath, swelling in the legs, confusion, fatigue, nausea, and decreased urine output can be the main symptoms of ARI [1]. The causes of renal diseases include excessive use of sodium, food additives, pain killers, low fluid intake, sedentary lifestyle and many diseases like hypertension and diabetes. The pathological indication of many renal diseases is Glomerulosclerosis and Renal fibrosis [2].Corn Silk, female flower of maize that has a yellowish thread-like strands is appreciable in history for the treatment of urinary tract infections, asthma, hypertension, dropsy, and pathological swelling. Many countries of the world like the United States, Turkey, China, and Serbia have been using corn silk to treat kidney stones, prostate disorders, edema, cystitis, urinary tract infections obesity, bedwetting, and diuretic. According to recent researches, corn silk promotes the flow of bile, causes a reduction in hyperglycemia, causes inhibition of IgE formation by glycoproteins, and possess anti-tumor effect and neuroprotective effects against oxidative stress, as well as has anti-fatigue activity by suppressing the production of blood lactic acid in animals. Corn silk is an effective natural-based treatment to cure oxidative stress and related diseases [3]. Corn silk (Maydis stigma) has tremendous medicinal properties and can be an inexpensive component of plant diet [4]. A significant potassium content that is present in corn silk is useful to treat urinary tract infections, formation of kidney stones and to relieve existing stones [5]. Corn silk has phytochemicals that are beneficial for health because of their anti-oxidant activity.

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Therefore, many diseases can be prevented by its use as a food additive and dietary fiber. Corn silk is a rich source of natural antioxidants and poly-phenolic compounds that have strong free radical scavenging activity. Many bioactive compounds are present in corn silk such as vitamins, carbohydrates, magnesium, proteins, calcium, sodium and magnesium salts, alkaloids, steroids and volatile salts, potassium, flavonoids and many other phenolic compounds that are beneficial for health. The mechanism of action and properties are related to potential use of bioactive components of corn silk such as terpenoids and flavonoids [6]. The most common cause of ARI is the excessive use of drugs. Drug-induced nephrotoxicity can have some risk factors related to patients that include the age of 60 years or more, heart injury, diabetes, sepsis volume depletion and underlying renal insufficiency (e.g. the rate of glomerular filtration <60ml / min / 1.73m2) [7]. In critically ill patients, nephrotoxic drugs cause severe ARI up to 25% of all cases [8]. The kidneys are at high risk of drug-induced damage because of high relative blood flow. The use of gentamicin is among the leading causes of drug-induced nephrotoxicity [9]. The application of gentamicin (GM) is well known for developing Acute Kidney Injury (AKI)[10]. GM is an aminoglycoside antibiotic used in the treatment of gram-negative bacterial infections. The use of such antibiotics can lead to the acute toxicity of kidneys. About 10-30% of patient experiences ARI induced by gentamicin [11]. Patients with renal disease can have a low life expectancy, including heart disease complications and severe kidney failure, leading to dialysis [12]. According to WHO, renal diseases are among the dominant causes of death. The rise in the ranking of kidney diseases among the main causes of death from 13th to 10th has been seen. The mortality rate of renal disease has increased to 1.3 million in 2019 from 813 000 in 2000 [13]. AKI affects 13.3 million people all over the world and causes over 2 million deaths annually. It is directly related to life quality and mortality risk. According to recent studies, 22% of all inpatients and 50% of critical patients induce ARI [14]. About 180 million population in Pakistan are prone to chronic diseases like hypertension, diabetes, and reduced renal reserve [15]. The patients in the intensive care Unit are more prone to develop acute kidney injury and nearly 30-50% of patients cannot survive [16]. ARI can be treated by the use of phytochemical compounds and natural products with a strong inhibitory effect on these mechanisms [5].

METHODS

White albino male rats were purchased from the Institute of Molecular Biology and Bio-Technology, University of Lahore. Gentamicin was purchased from local market in Lahore, Pakistan. The fresh Silk of Corn (Maydis Stigma) was Harvested from Chak no 425 J.B, Purana Wahla, a rural area in the district Toba Tek Singh, the Province Punjab, Pakistan. Preparation of Corn Silk Extract: To prepare the methanolic extract, 100 g of Corn Silk sample was soaked in 1000 ml of 80% methanol and shook in orbital shaker for 72hours. After 72h (3 days) the extract was filtered to separate the Corn Silk and Extract. The filtered extract was poured into falcon tubes and placed in a centrifuge machine for centrifugation. Once the centrifugation was done, the extract was evaporated until dry by using a rotary evaporator. An adequate amount of extract was being prepared by following the same method many times. The prepared extract was stored in clean and dried bottles that were placed in a desiccator. The stock solution of the extract was prepared by dissolving 25 g of extract in 50 ml of distilled water to prepare a 500 mg/ml concentration [11]. Experimental Design: 6-8 weeks old white albino male rats having weight of 200-250 g were adjusted to the conditions by providing them with basal diet for a period of one week. The environmental conditions like humidity (55±5%) and temperature (23±2%) were sustained during the entire study duration. All the animals received human care throughout and this protocol was authoritative by the ethical committee of The University of Lahore, Pakistan. ARI was induced to all rats by 100mg/kg/day Gentamicin administration for 7 days. After the induction of ARI all the rats were randomly divided into 3 groups (6 rats each group).

1. G0 Group: 0.1 ml/kg Isotonic Saline per day i.p were given to rats for 21 days.
2. G1 Group: 200 mg/kg Corn Silk Extract per day i.p were given for 21 days.
3. G2 Group: 300 mg/kg Corn Silk Extract per day i.p were given for 21 days.

Sample collection and bio-chemical assay: On 28th day, all the rats were sacrificed under light anesthesia and blood samples were collected for the determination of Serum Creatinine and Serum Urea.

RESULTS

The Serum Urea Levels of all the rats were evaluated on 0 Day, 8th Day, 20th Day and 28th Day and shown in table 5.3. The results showed that the consumption of Corn Silk extract causes a significant reduction in Serum Urea Levels in G2 and G3 as compared to G0. The current study observed that the Serum Urea levels of all rats before the start of the study were normal. The administration of GM caused a significant increase ($p < 0.001$) in levels of Serum Urea. After the induction of ARI, all the rats showed elevated Serum Urea Levels i.e ≥ 10-50mg/dl which confirmed the induction of disease. G1 Serum levels of Urea

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on 0th day were 27.8 ± 1.2 mg/dl and after administration of GM, it was elevated up to 80.3 ± 2.2 mg/dl. G2 Serum levels of Urea on the 0th day were 27.3 ± 1.52 mg/dl and after administration of GM, it was elevated up to 79.6 ± 2.56 mg/dl. On the 20th day, the recorded values showed that the Serum Urea Levels of G0 rats kept increasing because no treatment was given, all the rats of G1and G2 showed a reduction in Serum Urea Levels. On the 28th day, all the rats of G1 and G2 showed a reduction in Serum Urea Levels that were successfully treated with Corn Silk (200mg/kg and 300mg/kg respectively). Administration of Corn Silk Extract at both concentrations. Caused a significant decrease ($p < 0.0001$) in Serum Urea level as compared to the Control group.

Groups	0 Day (Serum Urea)	8th Day (Serum Urea)	20th Day (Serum Urea)	28th Day (Serum Urea)
Group 0 (G0)	29.5± 3.6	79.5± 7.74	87.8 ± 6.8	92.3 ± 7.2
Group 1 (G1)	27.8 ± 1.2	80.3 ± 2.2	59 ± 2.19	42.1 ± 2.3
Group 2 (G2)	27.3 ± 1.52	79.6 ± 2.56	52.3 ± 2.95	23 ± 4.0

Table 1: Serum Urea Mean (mg/dl) ± SD
(Mean Value for Serum Urea of G0, G1 and G2 Rats on 0th, 8th, 21st and 28th day)

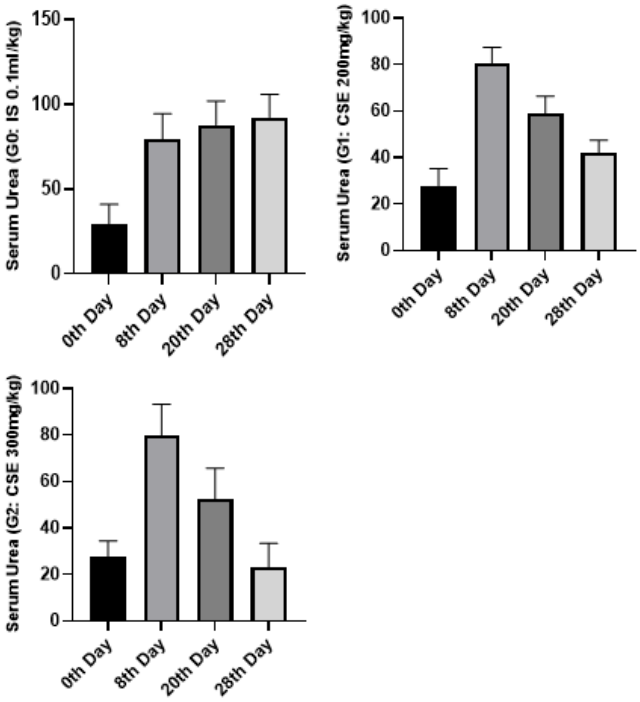

Figure 1: Serum urea levels of all groups has been represented in different graphs. G0 received isotonic saline 0.1ml/kg, G1 received CSE 200mg/kg, G2 received 300 mg/kg body weight on 8th, 20th and 28th day. Results are expressed as Mean ± SEM of all the groups in different graphs.

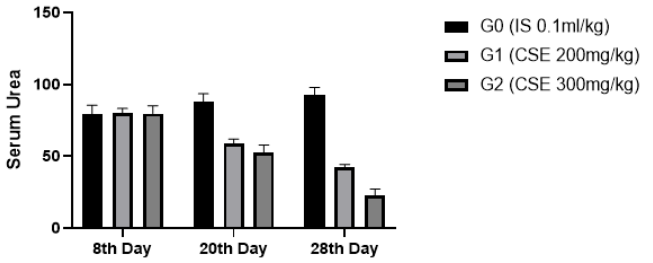

Figure 2: Graph represents the change in Serum Urea and the effect of different concentrations of CS extract on experimental groups (G1,G2) and isotonic saline on Control group during the treatment of Gentamicin induced ARI in rat models. G0 received isotonic saline 0.1ml/kg, G1 received CSE 200mg/kg, G2 received 300 mg/kg body weight on 8th, 20th and 28th day. Results are expressed as Mean ± SD of three different groups. P-value i.e $P < 0.01$ showed highly significant results.

The Serum Creatinine Levels of all the rats were evaluated at 0 Day, 8th Day, 20th Day and 28th Day and shown in table 5.4. The results showed that the consumption of Corn Silk extract causes a significant reduction in Serum Creatinine Levels in G2 and G3 as compared to the G0. The current study observed that the Serum Creatinine levels of all rats before the start of study were normal. The administration of GM caused a significant increase ($p < 0.001$) in levels of Serum Creatinine. After the induction of AKI, all the rats showed elevated Serum Creatinine Levels i.e ≥ 10-50mg/dl that confirmed the induction of the disease. G1 Serum levels of Creatinine on 0th day were 0.99 ± 0.00 mg/dl and after administration of GM, it was elevated up to 1.26 ± 0.69 mg/dl. G2 Serum levels of Creatinine on 0th day were 0.65 ± 0.16 mg/dl and after administration of GM, it was elevated up to 1.63 ± 0.069 mg/dl. On the 20th day, the recorded values showed that the Serum Creatinine Levels of G0 rats kept increasing because no treatment was given, all the rats of G1and G2 showed reduction in Serum Creatinine Levels. On 28th day, all the rats of G1 and G2 showed reduction in Serum Creatinine Levels that were successfully treated with Corn Silk (200mg/kg and 300mg/kg respectively). Administration of Corn Silk Extract at both conc. caused significant decrease ($p < 0.0001$) in Serum Creatinine level as compared to Control group.

Groups	0 Day (Serum Creatinine)	8th Day (Serum Creatinine)	20th Day (Serum Creatinine)	28th Day (Serum Creatinine)
Group 0 (G0)	0.57 ± 0.063	1.53 ± 0.04	1.61 ± 0.17	1.67 ± 0.01
Group 1 (G1)	0.99 ± 0.00	1.26 ± 0.69	1.27 ± 0.02	1.11 ± 0.05
Group 2 (G2)	0.65 ± 0.16	1.63 ± 0.069	1.29 ± 0.04	1.05 ± 0.26

Table 2: Serum Creatinine Mean ± SD
(Mean Value for Serum Creatinine of G0, G1 and G2 Rats on 0th, 8th, 21st and 28th day)

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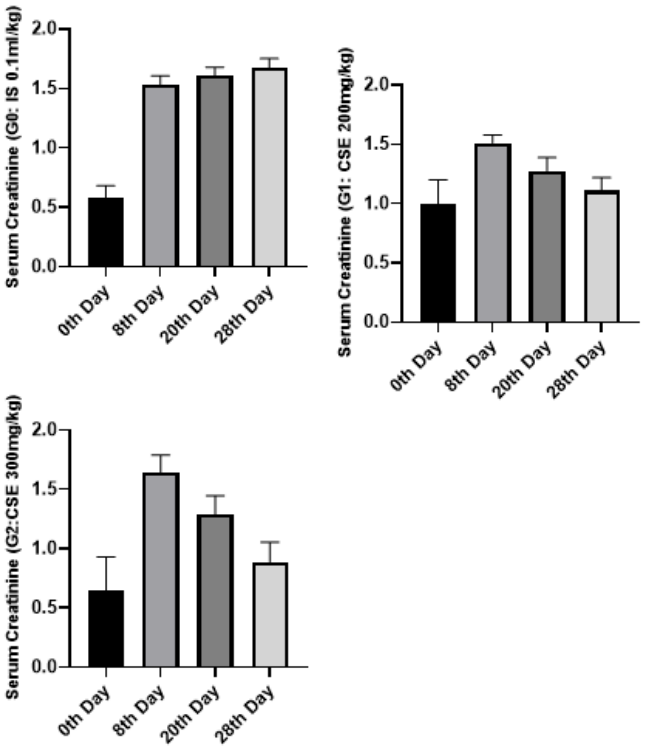

Figure 3: Serum Creatinine levels of all groups has been represented in different graphs. G0 received isotonic saline 0.1ml/kg, G1 received CSE 200mg/kg, G2 received 300 mg/kg body weight on 8th, 20th and 28th day. Results are expressed as Mean ± SEM of all the groups in different graphs.

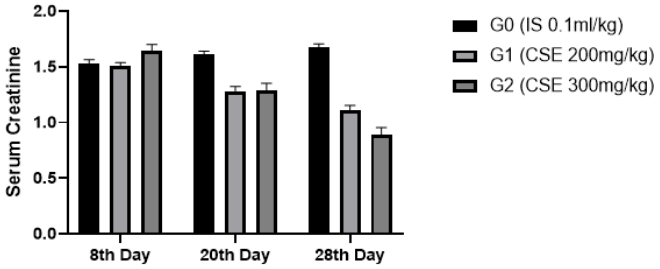

Figure 4: Graph represents the change in Serum Creatinine and the effect of different concentrations of CS extract on experimental groups (G1,G2) and isotonic saline on Control group during the treatment of Gentamicin induced ARI in rat models. G0 received isotonic saline 0.1ml/kg, G1 received CSE 200mg/kg, G2 received 300 mg/kg body weight on 8th, 20th and 28th day. Results are expressed as Mean ± SD of three different groups. P-value i.e $P < 0.01$ showed highly significant results.

DISCUSSION

In this study, the body weight, levels of serum urea and serum creatinine were significantly reduced. Previous studies [11,20] also supported these results. Several previously conducted studies has revealed that free radicals are observed to be a strong mediator of ARI induced by Gentamicin [17,18]. Renal dysfunction and proximal tubule injury causes drug storage in tubule cells as well as its interference with basolateral membranes and brush borders [19]. The results taken on the 28th day of the study observed that Corn Silk administered groups (G1 and G2) showed a notable reduction in Serum Urea (42.1±2.3 and 23±4.0), and Serum Creatinine (1.11±0.05 and 1.05±0.26). A study by Sepehri G et al. 2011 evaluated the effect of different doses of Corn Silk in Gentamicin induced nephrotoxicity. According to the results, it was seen that 200mg/kg & 300mg/kg of Corn Silk extract causes a significant reduction in levels of Urea (38.4±5.9 and 36.1±4.9 respectively) and Creatinine (0.55±0.08 and 0.58±0.11 respectively) [11]. Wans EM et al. 2021 reported a study in which methanolic extract of Corn Silk was evaluated in acetaminophen-induced nephrotoxicity in rat models. It was concluded that Corn Silk methanol extract reduced urea (35.15±2.29) and creatinine levels (0.38±0.045) [20]. This study shows that Corn Silk methanol extract has potent renal protective potential which is mediated by its antioxidant properties due to the presence of important phenolic compounds. The current study also confirms the use of corn silk in weight reduction as well as improvement of renal functions.

CONCLUSIONS

The results of this study showed that Corn Silk extract has significantly reduced Serum Urea and Serum Creatinine levels. The present study highlights the therapeutic potential of Corn Silk in ARI induced by Gentamicin in rat models. The previous studies have manifested the tremendous bioactivities of Corn Silk as glucose-lowering, anti-oxidant, anti-fatigue, anti-depressant, and diuretic agent. Therefore, it is crucial to encourage new researches, so that more beneficial effects of Corn Silk can be discovered. For a clinical point of view, innovative trials with high-quality methods are required to discover more pharmacological activities of Corn Silk.

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