Hematoprotective Effect of Naringin on 5-FU Toxicity in Rats

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Abstract 5-FU, an anticarcinogenic agent, is reported to have side-effects that include hemotoxicity. The study objective was to investigate the hemaprotective effects of naringin on 5-FU-induced toxicity. Thirty rodents were assigned to three groups. The control group received 1 ml of intragastric distilled water for 14 days. The 5-FU group received 1 ml of distilled water for 14 days as a placebo. On day 9, this same group received a 20 mg/kg dose of 5-FU administered intraperitoneally (IP) for a further five days. The naringin+5-FU group received a 100 mg/kg dose of naringin (IP) for 14 days. On day 9, 20 mg/kg of 5-FU was administered (IP) to this group for a further five days. On day 15, the rats were decapitated, and blood was taken. It was determined that Hematological parameters like Red Blood Cells (RBCs), White Blood Cells (WBC) count, Hemoglobin (Hb) concentration, hematocrit were significantly elevated in the 5-FU group, compared to the control group. The comparative values were similar in the control and naringin+5-FU groups. Naringin was observed to have a hemoprotective effect on 5-FU-induced toxicity.

Keywords 5-FU, Rat, Naringin, Hematoprotective

Introduction
5-FU is widely used as chemotherapy for various cancers [1]. As a fluoropyrimidine antimetabolite agent, it plays an important role in the treatment of colon, breast, gastrointestinal, head, neck and pancreatic cancer [1]. However, serious toxicity and unwanted side-effects occur following its use [2]. In addition, it has hemotoxic effects [3,4]. A number of studies have been conducted on the use of natural therapies to avoid the side-effects of anticancer agents [5-9]. Naringin is a flavonoid that is usually found in grapefruit, orange and cooked tomato paste [10]. It has antioxidant, immunomodulatory and anti-inflammatory properties. Flavonoids may have a protective effect against disease through various mechanisms, \emph{i.e.}, by activating and protecting antioxidant enzymes in the cells [11]. Naringin was reported in various studies to be protective against hematoxicity [12, 13]. The objective of the current study was to evaluate the Hematoprotective potential of naringin against 5-FU-induced toxicity.

Materials and Method
The objective of the study is to evaluate the deleterious effects of Naringin on hematological parameters protective effect of flavonoid naringin on rats. Spraque dawley rats were divided into three different groups (Table 1). The control group received 1 ml of intragastric distilled water for 14 days. The 5-FU group received 1 ml of distilled water for 14 days as a placebo. On day 9, this same group received a 20 mg/kg dose of 5-FU administered intraperitoneally (IP) for a further five days. The naringin+5-FU group received a 100 mg/kg dose of naringin (IP) for 14 days. On day 9, 20 mg/kg of 5-FU was administered (IP) to this group for a further five days. On day 15, the rats were decapitated, and blood was taken.
Determination of Hematological Parameters

Hematological parameters like Red Blood Cells (RBCs), White Blood Cells (WBC) count, Hemoglobin (Hb) concentration, hematocrit were measured by electronic automated blood cell coulter.

### Table 1: All groups of study and animal protocols

<table>
<thead>
<tr>
<th>Groups</th>
<th>The number of animals in groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
</tr>
<tr>
<td>5-FU</td>
<td>10</td>
</tr>
<tr>
<td>Naringin+ 5-FU</td>
<td>10</td>
</tr>
</tbody>
</table>

### Statistical Analysis

All data were statistically evaluated by one-way ANOVA using SPSS 20.00. The data were expressed as mean ± SD. \( P < 0.05 \) was considered statistically significant.

### Results

In this present study significant differences in the haematological parameters were observed in 5-FU induced rats compared to control and Naringin+5-FU groups rats. The total number of RBC, hemoglobin, hematocrit, WBC were significantly decreased (Figure 1 A, B, C and D, \( p<0.05 \)) in 5-FU-induced rats.

![Figure 1: Effects of 5-FU and naringin on hematological parameters in control and experimental group of rats.](image)

**Figure 1:** Effects of 5-FU and naringin on hematological parameters in control and experimental group of rats.

- **RBC:** Red blood cell
- **WBC:** White blood cell
- **Hb:** Hemoglobin
Discussion
The hematopoietic system is one of the most sensitive systems that assess the harmful effects of drugs on living organisms [14]. In this study, it has been shown that 5-FU has a significant adverse effect on hematological parameters in rats and that pre-treatment with naringin successfully improves hematological disorders caused by 5-FU. The toxic effect of 5-FU on blood parameters was demonstrated by the significant reduction in RBCs and decline in the values of Hb, HTC, WBCs were recorded in 5-FU-treated rats as well. Such a relationship may be due to different reasons, including the destruction of bone marrow cells or the enhancement of the osmotic fragility of RBCs. Thus, 5-FU poisoning represses the activity of hematopoietic tissues, disrupts erythropoiesis and may lead to accelerated RBC breakdown anemia due to altered RBC membrane permeability, increased RBCs mechanical brittleness and impaired Fe metabolism. While cell proliferation is slowly decreased, the anticancer effect is not significantly enhanced at high doses of 5-FU [15]. Therefore, to alleviate bone marrow suppression by 5-FU, natural products like Naringin preferred for promoting hematopoiesis, proliferation and differentiation of myeloid progenitor cells. Our hematologic results showed that 5-FU dramatically affects blood parameters, signifying severe cytopenia in rat. Whereas naringin administration significantly increased the WBC level.

In conclusion, we propose that naringin administration inhibits 5-FU-induced hematoxicity in this study.

References
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