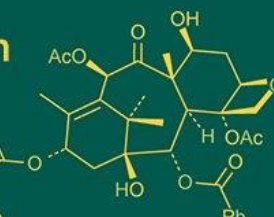


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Evaluation of body weight in cerulein-induced acute pancreatitis in swiss albino mice following umbelliferone pretreatment

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Abstract

The present study was undertaken to evaluate the ameliorative effects of umbelliferone in cerulein-induced acute pancreatitis. A total of 30 Swiss albino mice (6-8 weeks old) were procured, maintained under standard laboratory conditions, and acclimatized for one week. The animals were randomly divided into five groups, each consisting of six mice, and the study was carried out over a period of seven days. The sham control group received normal saline intraperitoneally, while the disease control group was administered cerulein (50 µg/kg body weight) intraperitoneally in six doses at one-hour intervals on day 7. The umbelliferone control group received umbelliferone (60 mg/kg body weight, orally) once daily for seven days. Another group was pretreated with umbelliferone (60 mg/kg body weight, orally) for seven consecutive days, followed by cerulein administration (50 µg/kg body weight, intraperitoneally, six doses at one-hour intervals) on day 7. The standard treatment group received dexamethasone (10 mg/kg body weight, intraperitoneally) daily for seven days along with a cerulein challenge on day 7. On the final day of the experiment, body weights were recorded and analyzed. No significant changes in body weight were observed among the groups compared to the normal control group ($p < 0.05$), suggesting that the short experimental duration and the acute nature of cerulein-induced pancreatitis that did not produce marked effects on overall body weight.

Keywords: Cerulein, Umbelliferone, swiss albino, body weight

Introduction

Acute pancreatitis (AP) is an inflammatory condition of the pancreas and represents one of the most common causes of hospital admission among gastrointestinal disorders worldwide (Lankisch *et al.*, 2015) [1]. The global incidence of AP has been steadily rising, and nearly 20% of patients develop severe forms of the disease that are associated with considerable morbidity and mortality (Lund *et al.*, 2006, Rau *et al.*, 1997) [2, 3]. The condition is characterized by sudden pancreatic inflammation accompanied by elevated levels of digestive enzymes in the bloodstream, including amylase and lipase, even in the absence of specific therapeutic intervention (Spanier *et al.*, 2008) [4].

The complications associated with AP are largely related to systemic inflammatory responses and dysfunction of vital organs. Patients with severe pancreatitis may develop complications such as cardiogenic shock, renal and respiratory insufficiency, cardiac dysfunction, and hepatic injury. In advanced cases, the inflammatory process may extend beyond the pancreas and lead to failure of distant organs, ultimately resulting in multiple organ dysfunction syndrome (Lankisch and Banks, 2013) [5]. AP is characterized by interstitial edema, cellular vacuolization, inflammatory infiltration, and necrosis of pancreatic acinar cells. The disease is commonly triggered by factors such as excessive alcohol intake, biliary tract disorders, certain medications, and invasive procedures involving the pancreatic and biliary ducts (Ho and Frey, 1995, Beger *et al.*, 1997) [6, 7].

Experimental animal models are widely employed to investigate the mechanisms underlying pancreatic injury and to evaluate potential therapeutic agents. Among the available models, cerulein-induced acute pancreatitis is a widely used experimental model for investigating the pathogenesis of pancreatitis and the associated damage to multiple organs (Frossard *et al.*,

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1999) [8]. Cerulein, a cholecystokinin analogue, when administered at supramaximal doses (50 µg/kg in mice), induces a mild and reversible form of pancreatitis that closely resembles several biochemical and histopathological features of the human disease (Yamaguchi *et al.*, 1989) [9]. This model is particularly valuable because it rapidly produces oedematous pancreatitis accompanied by increased serum amylase and lipase levels, oxidative stress, inflammatory responses, and activation of nuclear factor-κB (NF-κB) signaling pathways (Huang *et al.*, 2013) [10].

During experimental studies, body weight is routinely monitored as an indicator of the overall health status and metabolic condition of laboratory animals, and may reflect the systemic effects of disease induction and treatment.

Umbelliferone (UMB) also known as 7-hydroxycoumarin, is a naturally occurring coumarin derivative present in several plant species including coriander, carrot, and garden angelica (Mazimba, 2017) [11]. Previous investigations have demonstrated that UMB possesses a variety of pharmacological activities, including antioxidant, anti-inflammatory, and anti-apoptotic effects (Gan *et al.*, 2018, Germoush *et al.*, 2018) [12, 13]. These biological properties suggest that umbelliferone may offer protective benefits in inflammatory conditions associated with oxidative stress. However, the protective role of umbelliferone in cerulein-induced AP remains unclear. Therefore, this study aimed to evaluate its effects, with emphasis on body weight as an indicator of the animal's physiological status.

Materials and Methods

Chemicals

Cerulein was obtained from Sigma-Aldrich and Umbelliferone was obtained from Tokyo Chemicals Industry Co., Ltd.

Experimental Animals

Thirty male Swiss albino mice (6-8 weeks old) weighing 22-30 g were obtained from Jeeva Life Sciences, Hyderabad, India. The animals were housed in a clean environment maintained at an ambient temperature of 22-24 °C with a 12 h light/dark cycle. Before the initiation of the study, mice were acclimatized for a period of seven days. Throughout the experiment, animals received standard laboratory pellet feed and had free access to water. The study was performed in accordance with CPCSEA guidelines.

Experimental Design

The mice were randomly divided into five groups, with six animals in each group and treated according to the experimental protocol for a duration of 7 days. The selected doses of umbelliferone and cerulein were adopted from existing literature reports.

1. Normal control: Animals received normal saline i.p. for 7 consecutive days.
2. Cerulein control: Animals were administered cerulein (50 µg/kg, i.p.) in six injections at 1-hour intervals on day 7.
3. Umbelliferone (UMB): UMB (60 mg/kg, p.o) was administered for 7 days.
4. Umbelliferone + Cerulein group: Animals were pretreated with UMB (60 mg/kg, p.o), followed by administration of cerulein (50 µg/kg, i.p.) in six injections at 1-hour intervals on day 7.

5. Dexamethasone + Cerulein: animals were pretreatment with dexamethasone (10 mg/kg, i.p.) for 7 days, followed by administration of cerulein (50 µg/kg b.w., i.p.) in six injections at 1-hour intervals on day 7.

Monitoring of body weight

Body weights of all animals were recorded on day 7 using a digital balance (Shimadzu Pvt. Ltd) to assess differences among the experimental groups.

Statistical analysis

Data were expressed as Mean ± SEM and analyzed statistically using on-way analysis of variance (ANOVA), followed by Duncan's post hoc test for intergroup comparisons (n = 6 animals per group). Statistical analysis was performed using IBM SPSS Statistics version 21.0. Differences were considered statistically significant at $p < 0.05$.

Results

Body weights

The body weights of animals in the different groups remained unchanged, with no significant difference compared to the normal control group. The results are presented in Table 1 and Fig. 1.

Table 1: Average body weight (g) of different groups of mice

Group	Day 7
1. Normal Control	23.36±0.87
2. Cerulein Control	20.54±1.05
3. Umbelliferone Control	22.96±0.91
4. Umbelliferone + Cerulein	23.89±1.03
5. Dexamethasone + Cerulein	23.58±1.18

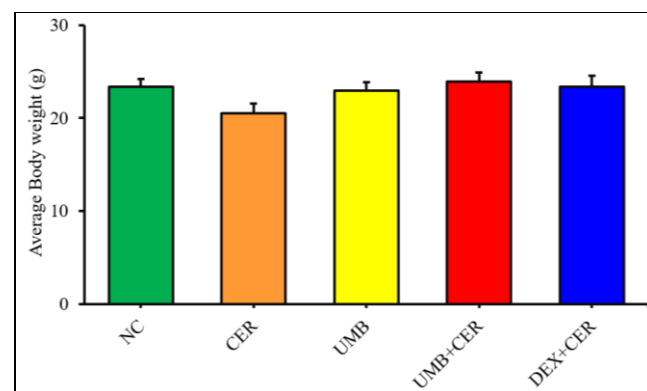


Fig 1: Effect of umbelliferone on body weight.

Discussion

Acute pancreatitis is an inflammatory disorder characterized by a broad spectrum of clinical manifestations, ranging from a mild, self-limiting condition in most cases (75-80%) to a severe form that can lead to multisystem organ failure, sepsis, and mortality (Wu, 2000) [14]. Current treatment approaches mainly focus on alleviating pain, controlling inflammation, and managing related infections (Greenberg *et al.*, 2016) [15].

Cerulein-induced pancreatitis is a commonly used experimental model that reproduces several pathological features observed in human acute pancreatitis (Gorelick *et al.*, 1993) [16].

Phytocostituents possess antioxidant and anti-inflammatory properties, which may be beneficial in the management of

inflammatory diseases (Allawadhi *et al.*, 2018) ^[17]. In the present study, umbelliferone was selected to evaluate its protective effect against cerulein-induced acute pancreatitis. UMB is a naturally occurring coumarin that is widely found in members of the Rutaceae and Asteraceae families (Mazimba, 2017) ^[11].

In the present study, body weight remained comparable among all experimental groups throughout the experimental period. The absence of significant changes suggests that induction of acute pancreatitis by cerulein did not markedly influence the overall metabolic or nutritional status of the animals. In this experimental model, cerulein was administered as six intraperitoneal injections on the seventh day following pretreatment, and the animals were sacrificed six hours after the final injection. The relatively short interval between pancreatitis induction and sacrifice may explain the lack of noticeable alterations in body weight, as systemic effects influencing body mass generally require a longer duration to become evident. Similar findings have been reported in previous studies using cerulein-induced acute pancreatitis models, where body weight remained largely unaffected during the short experimental period (Bansod *et al.*, 2021) ^[18]. Furthermore, pretreatment with umbelliferone did not result in any significant increase or decrease in body weight, indicating that the compound was well tolerated and did not produce adverse effects on the physiological condition of the animals. These observations suggest that both the experimental induction protocol and umbelliferone treatment did not compromise the general health status of the animals during the study period.

Conclusion

Overall, the absence of significant changes in body weight across all groups, including those administered cerulein (50 µg/kg b.w., i.p), indicates that the experimental procedures and treatments were tolerated and did not induce systemic toxicity. This stability further supports that the observed effects are not confounded by alterations in general physiological status.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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