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Aim and Objective: The main aim of the study is to evaluate the possible histological effects of aqueous stem bark extract of Cadaba farinosa on the gastrointestinal tract of Wistar rats.

Materials and Methods: The lethal dose (LD50) of aqueous stem bark extract of Cadaba farinosa was determined using the Lorke's method. Thirty (30) male and female Wistar rats were selected and randomized into five groups of six rats per group. Group 1 served as the control group, and no extract was administered to the experimental animals while the rats in groups 2, 3, 4, and 5 were administered by gavage dose levels 100, 200, 300, and 400 mg/kg extract for twenty-eight days.

Keywords: *cadaba farinosa, stem bark, wistar rats, intestinal goblet cells, mucin, and cyclooxygenase.*

GJMR-B Classification: *NLMC Code: QV 4*



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Histological Effects of Aqueous Stem Bark Extract of *Cadaba Farinosa* on Gastrointestinal Tract of Wistar Rats

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Abstract- ***Background:*** *Cadaba farinosa fork* is widely used traditionally as mucosae plant medicine for treatments of diarrheal, dysentery, intestinal parasites, and ulcerative peptic diseases that are hard to cure even with conventional medicines.

Aim and Objective: The main aim of the study is to evaluate the possible histological effects of aqueous stem bark extract of *Cadaba farinosa* on the gastrointestinal tract of Wistar rats.

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Result: The lethal dose (LD_{50}) of aqueous stem bark extract of *Cadaba farinosa* is above 5000mg/kg. Sub-chronic oral administration of aqueous stem bark extract of *Cadaba farinosa forsk* at the tested doses showed numerous intestinal goblet cells that secrete mucin and cyclooxygenase.

Conclusion: Acute oral administration of aqueous stem bark extract of *Cadaba farinosa forsk* is safe up to 5000mg/kg body weight/day. Sub-chronic oral administration of aqueous stem bark extract of *Cadaba farinosa forsk* at the tested doses showed numerous intestinal goblet cells that secrete mucin and cyclooxygenase (COX) responsible for the synthesis of prostaglandin. Hence, *Cadaba farinosa forsk* is a possible source of anti-peptic ulcer drug since prostaglandins deficiency plays a critical role in the background of gastrointestinal lesions.

Keywords: cadaba farinosa, stem bark, wistar rats, intestinal goblet cells, mucin, and cyclooxygenase.

I. Introduction

A peptic ulcer disease is major diseases of the gastrointestinal tract seen throughout the world[1]. The formation of peptic ulcer diseases depends on the presence of acid and peptic activity in gastric juice with a breakdown in mucosal defenses of the gastrointestinal tract[2]. The prevalence of Helicobacter pylori infection and widespread use of acetylsalicylic acid and other nonsteroidal anti- inflammatory drugs (NSAIDs) are known etiologic agents disrupting mucosal resistance to injury[3,4]. Several other pathogenic elements postulated for gastrointestinal lesions, include prostaglandins deficiency, bile acids, bacterial flora, and nitric oxide[5,6], yet the precise mechanisms remain unknown.

Currently, the prevention and cure of peptic ulcer diseases are among global health challenges confronting medicine[2]. In our review, most reported studies give the general idea of peptic ulcer and its management using synthetic drugs demonstrated intermittent relapses and adverse drug interactions[7,8,9].

However, many medicinal plants have been reported to possess beneficial effects in gastrointestinal disorders, especially ulcerative peptic diseases with a high level of safety compared to most synthetic drugs[10]. In developing countries, most people still rely on medicinal plants to meet their health needs, especially in cases where synthetic medicines could not provide relief from hard-to- cure illnesses[11,12]. *Cadaba farinosa* belongs to the capparidaceae (capparaceae) family[13]. The plant is enriched with abundant phytochemicals, including flavonoids and alkaloids are widely used in traditional medicine as antibacterial, antiprotozoal and anthelminthic agents to treats diarrheal, dysentery, and gastrointestinal parasites[13,14]. The stem bark of *Cadaba farinosa* served as aperients, purgative, and stomachic stimulants. In that desert of India and Pakistan, its extract is externally applied to fresh wounds to prevent sepsis, thereby assisting in healing[15,16]. In Nigeria, the analgesic and anti-inflammatory properties of *Cadaba farinosa* was reported among the people of Maiduguri, Jimeta, and Nguru[17].The plant was also used in the management of gastric and duodenal ulcers by inhibition of carbonic anhydrase[18].Hence, these findings prompted us to study the possible histological effects of the aqueous stem bark extract on the gastrointestinal tract.

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II. Materials and Method

a) Experimental Animals

Wistar rats were procured from the Animal House, Faculty of Pharmaceutical Science, Usmanu Danfodiyo University Sokoto, and maintained with free access to standard animal pellets and water. The permission and approval for animal studies with Reg. NO: PTAC/Cf/OT/004-18 was obtained from the Faculty of Pharmaceutical Sciences, Animal Ethics Committee, Usmanu Danfodiyo University Sokoto.

b) Plant Collection

The fresh stem bark of *Cadaba farinosa* was harvested from its natural habitat at the Faculty of Pharmaceutical Science, Usmanu Danfodiyo University Sokoto. The plant was authenticated and deposited at the Department of Pharmacognosy and Ethno medicine, Usmanu Danfodiyo University Sokoto, Nigeria.

c) Plant Extraction

The fresh inner stems bark was shadow dried and pounded into small pieces using pestle and mortar. About 210g powdered plant material was soaked and extracted in 600mL of water at room temperature for 24 hours[19]. The liquid filtrates were concentrated and evaporated to dryness at 45°C in a water bath. The aqueous extract was stored at -4°C until used.

d) Experimental Design

The acute toxicity and LD_{50} determination were carried out using Lorke's method[20]. According to guideline 423 of the Organization for Economic Cooperation and Development (OECD), the first phase consists of nine Wistar rats that were separated into three groups of three rats each and the aqueous extract was administered by gavage at dose levels 10, 100, and 1000 mg/kg/day. A cage side observation was done to detect any behavioral signs of toxicity salivation, erection of the hair, diarrhoea or mortality.

Following the absence of toxicity sign, the second phase according to Lorke's consisted of three rats that were administered with dose levels 1600, 2900, and 5000mg/kg/24 hours. The animals were observed for signs of toxicity.

In the sub-acute study, thirty (30) male and female Wistar rats were selected and randomized into five groups of six rats per group. Group 1 served as the control while the rats in groups 2, 3, and 4 were administered with plant extract by gavage at dose levels 100, 200, 300, and 400mg/kg for twenty-eight days.

Table 1: Acute toxicity study and LD_{50} determination of aqueous stem bark extract of *Cadaba farinosa* on Wistar rats (n=12)

Dose	Mortality	
mg/kg body weight	Phase I	Phase II
10		-
100		-
1000		-
1600	-	
2900	-	
5000	-	

e) Tissue Histology

The intestines of Wistar rats were excised by abdominal incision and the tissues were fixed in 10% formal saline for 24 hours before being processed and embedded in paraffin wax. The tissues were sectioned with a rotary microtome at 5μm, and the cut sections were stained with Haematoxylin and Eosin (H&E) stain[21]. The stained slides were carefully examined under a light microscope at high power magnification, and photomicrographs were taken[22].

III. Results

a) Acute toxicity and LD_{50} determination

The toxicity study and LD_{50} determination result (Table 2) showed that oral administration of the aqueous stem bark extract of *Cadaba farinosa* at dose levels 10, 100, 1000mg/kg/24hours produced no behavioral sign of toxicity or mortality.

In Phase II, oral administration of the extract at dose levels 1600, 2900, and 5000mg/kg/day, indicated neither behavioral change nor death. The animals were as active as control. Therefore, the median lethal dose (LD_{50}) of aqueous stem bark extract of *Cadaba farinosa* is above 5000mg/kg.

Table 2: Acute toxicity study following oral administration of aqueous stem bark extract of *Cadaba farinosa* on adult Wistar rats (n=12)

Dose	Mortality	
mg/kg body weight	Phase I	Phase II
10	0/3	-
100	0/3	-
1000	0/3	-
1600	-	0/1
2900	-	0/1
5000	-	0/1

b) Tissue effects of plant extract

Our histological finding showed normal intestinal goblet cells lined by epithelial cells and intact submucosa and smooth muscle layers (Plate 1).

Extract administration of 100mg/kg/28days showed considerably increased intestinal goblet cells lined by epithelial cells and well-preserved submucosa and smooth muscle layers (Plate 2).

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Extract administration of 200,300 and 400mg/kg/28 days showed numerous intestinal goblet cells, and well-preserved submucosa and smooth muscle layers (Plate 3, 4, and 5).

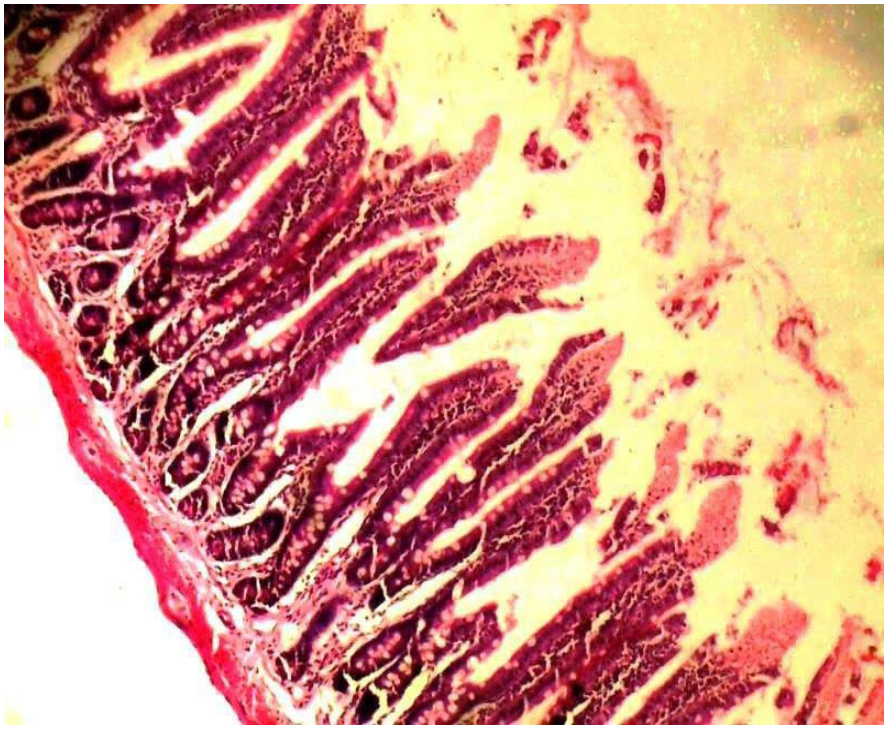


Plate 1: Normal control showed a mucosa layer with few intestinal goblet cells lined by epithelial cells and intact submucosa and smooth muscle layers. (H&E. X100).

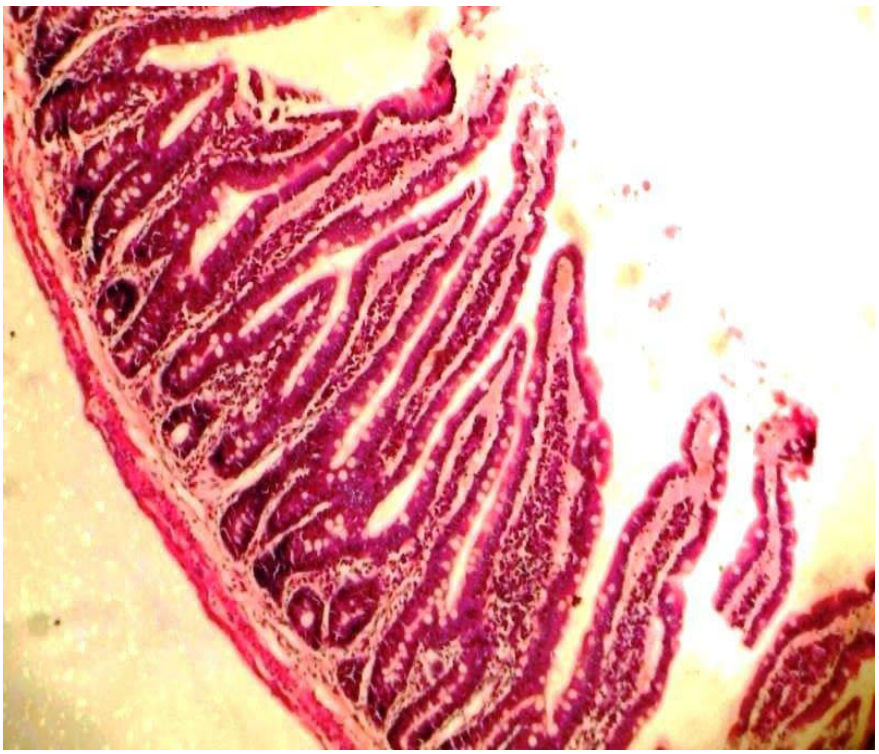


Plate 2: Administration of 100mg/kg/28days showed a mucosa layer with considerably increased intestinal goblet cells lined by epithelial cell and well- preserved submucosa and smooth muscle layers. (H&E. X100).

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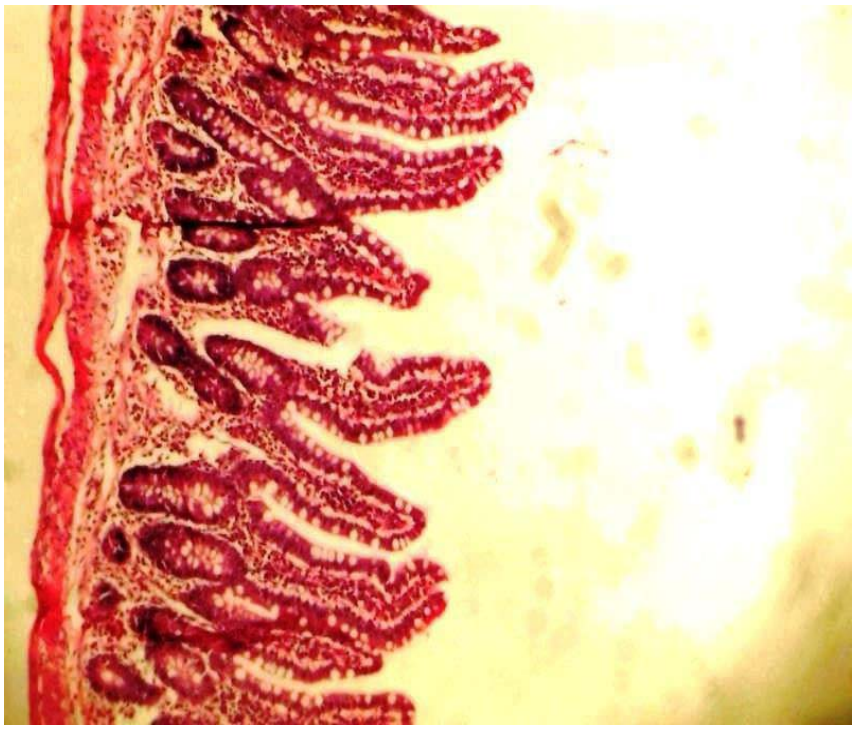


Plate 3: Administration of 200mg/kg/28days showed a mucosa layer with numerous intestinal goblet cells lined by epithelial cells and well-preserved submucosa and smooth muscle layers. (H&E. X100).

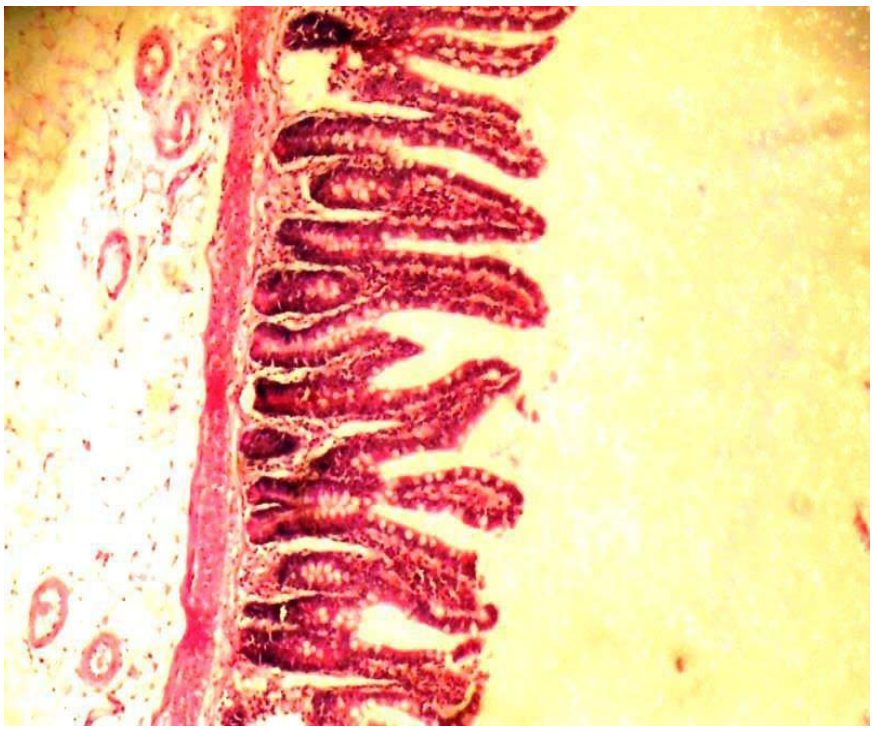


Plate 4: Administration of 300mg/kg/28days showed a mucosa layer with numerous intestinal goblet cells lined by epithelial cells, and well-preserved submucosa and smooth muscle layers. (H&E. X100).

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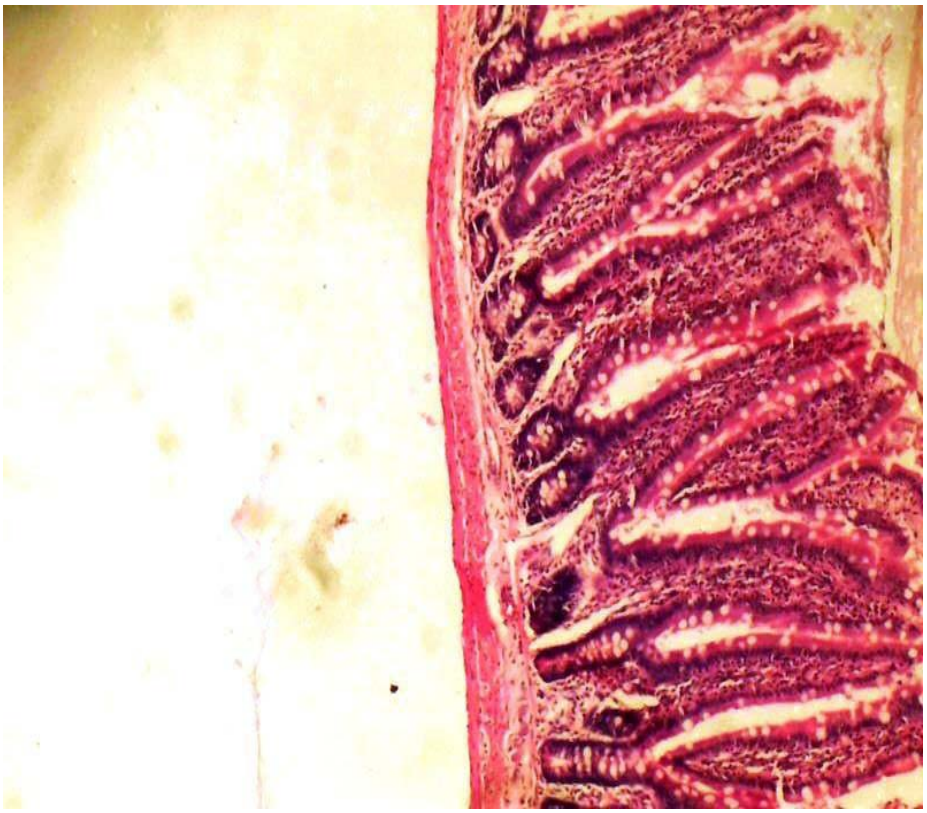


Plate 5: Administration of 400mg/kg/28days showed a mucosa layer with numerous intestinal goblet cells lined by epithelial cells, and well-preserved submucosa and smooth muscle layers H&E. X100).

IV. Discussion

Gastrointestinal lesions (ulcerative peptic diseases) is associated with several pathogenic elements, including prostaglandins deficiency, bile acids, bacterial flora, and nitric oxide,[5,6] yet the precise mechanisms remain unknown[23]. However, the overwhelming proportions of chemical agents (84.45%) used in most pharmaceutical industries for the production of conventional drugs used for the management of gastrointestinal lesions are gotten from plants[24]. In the present study, the acute toxicity study revealed that oral administration of *Cadaba farinosa* extract up to 5000mg/kg produced no immediate signs of toxicity or mortality indicating that the LD_{50} was above 5000 mg/kg, therefore, this explains that aqueous extract of *Cadaba farinosa* could be administered to animals with some degree of safety, through oral route where absorption might not be complete due to inherent factors limiting gastrointestinal tract absorption[25].

Our histological finding, showed a mucosa layer with few intestinal goblet cells lined by epithelial cells with intact submucosa and smooth muscle layers (Plate 1), while extract dose level 100mg/kg/28days showed considerably increased intestinal goblet cells and well-preserved submucosa and smooth muscle layers (Plate 2). A mucosa layer with numerous intestinal goblet cells that was lined by epithelial cells and well-preserved submucosa, and smooth muscle layers were seen in animals at dose levels 200, 300, and 400mg/kg compared to the normal control with few intestinal goblet cells.

Intestinal goblet cells are unicellular glands[26]. These cells synthesized and secretes mucin and cyclooxygenase (COX) responsible for the synthesis of prostaglandin that is expressed in cyclooxygenase pathway 1 (COX-1) and the inducible cyclooxygenase pathway 2 (COX- 2) isoforms[27]. The intestinal goblet cells following oral administration of aqueous stem bark of *Cadaba farinosa* is indicative of high secretion of mucin COX-2 that would preserve vulnerable cellular compartment of the gastrointestinal tract. The luminal prostaglandin modulates acid concentration by inhibiting acid secretion, alter blood flow, and stimulate mucus and bicarbonate secretion leading to dramatic protection against mucosal damage. Our result is similar to the role of endogenous prostaglandins in gastric secretion and mucosa defence[28], the anti-inflammatory effects of prostaglandins in ameliorating mucosal damage[26,27], and stimulation of duodenal bicarbonate and mucus secretion mediated intestinal mucosal protection[29,30,31]. These physiological functions of mucin COX-2 could modulate major etiologic factors implicated in ulcerative peptic diseases, including lesions caused by NSAIDs were effectively prevented by supplementation of exogenous prostaglandin-endoperoxide synthase (PGE2)[31,32,33].

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Therefore, stem bark extract of *Cadaba farinosa* is a possible source of a drug, which modulates secretions of mucus, acid, and bicarbonates preceding dramatic protection against mucosal damage risk factors of ulcerative peptic diseases and gastrointestinal hemorrhage.

V. Conclusion

This study showed that acute oral administration of aqueous stem bark extract of *Cadaba farinosa forsk* is safe up to 5000mg/kg body weight/day. Sub-chronic oral administration of aqueous stem bark extract of *Cadaba farinosa forsk* at the tested doses showed numerous intestinal goblet cells that secretes mucin and cyclooxygenase (COX) responsible for the synthesis of prostaglandin. Hence, *Cadaba farinosa forsk* is a possible source of anti-peptic ulcer drug since prostaglandins plays a critical role in the background of gastrointestinal lesions.

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Conflict of interest
None declared

Ethical approval
No: PTAC/Cf/OT/004-18 was obtained from the Faculty of Pharmaceutical Sciences, Animal Ethics Committee, Usmanu Danfodiyo University Sokoto.

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