Possible Healing Effects of Aloe Barbadensis on Nephrotoxicity Induced by Soybean Oil in Rats

Sıçanlarda Soya Yağı ile Oluşturulan Böbrek Hasarı Üzerine Aloe Barbadensis'in İyileştirici Etkileri

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Abstract
Purpose: This study aimed to analyze the effects of Aloe barbadensis on kidney.
Material and Methods: Eighteen Wistar Albino female rats were used for the experiment. They were divided into 3 groups. Biopsy materials were taken from the right kidneys of the rats and were analyzed under the light microscope.
Results: Biopsy materials, which were taken from the kidneys of the control subjects, revealed normal structural features of renal cortex and medulla. No distinctive difference was found in the Malpighi corpuscles in the group receiving Aloe Barbadensis. However, various degrees of vacuolization in the proximal tubules, and the complete loss of structural characteristics of proximal tubules were observed. Vacuolization was rarely seen in distal tubules. Congestion was clear in the medulla. In the third group receiving only soybean oil, a distinctive congestion was observed in all glomerulus and in the medulla. The detected pathologic changes were more common and severe in the third experiment group that received only soybean oil. Congestion in glomerulus was mostly observed in this group.
Conclusion: These results lead us to consider that Aloe barbadensis plays a healing role against the toxic effects of soybean oil on the kidney.

Key words: **Aloe vera; Cytoprotection; Kidney; Rat.**

Özet
Amaç: Bu çalışmada Aloe Barbadensis'in böbrek üzerine koruyucu etkilerinin araştırılması amaçlandı.
Gereç ve Yöntemler: Wistar Albino cinsi 18 dişi sıçan kullanıldı. Sıçanlar 3 eşit gruba ayrıldı. Ratların sağ böbreklerinin korteka ve medulla'sından biyopsi materyalleri alınarak ışık mikroskobik düzeyde incelendi.
Bulgular: Kontrol deneklerin böbreklerinden alınan biyopsi materyalleri incelendiğinde normal boyut ve yapıda Malpighi cisimcikleri gözlendi. Proksimal,distal tübüller ve medulla olağandı. Aloe barbandensis verilmiş grupta ise Malpighi cisimciklerinde belirgin bir farklılık görülmedi. Ancak proksimal tübüllerde değişen derecelerde vakuolizasyon ve sonuçta yapısal özelliklerini tamamen yitirmiş proksimal tübüller gözlendi. Distal tübüllerde ise nadiren vakuolizasyon görüldü. İnterstisyel alanda korteks ve medullada konjesyon vardı. Sadece soya yağının verildiği üçüncü grupta ise tüm glomerüllerde ve medullada belirgin konjesyon vardı. Proksimal tübüllerdeki değişiklikler de ikinci gruba göre daha yaygın ve şiddetli düzeyde idi.
Sonuç: Bu sonuçlar bize Aloe barbadensis'in, soya yağının böbrek üzerine olan toksik etkilerini iyileştirici rolü olduğunu düşündürmektedir

Anahtar Kelimeler: **Aloe vera; Böbrek; Hücrekoruma; Sıçanlar.**

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Introduction

Aloe Vera (AV), a very popular plant, has been used for alternative medicine and its gel form is mostly preferred (1). Its chemical and therapeutic properties have been recently investigated (2). AV contains anthraquinin, polysaccaride and carbohydrate. Anthraquinin is extracted from the plant before use (3). It's most active content is acemannan (4). Aloe Barbadensis (AB), one of the AV types, is the most common used form for commercially and also therapeutic purposes in North America, Europe, and Asia (5). Plants containing AB have been used as anti-inflammatory agents, for the treatment of ulcer, hepatitis and neoplasies, and also for wound healing (6). It has been reported that it stimulates macrophages and has antiviral effects (7). Antioxidative effects of AB have been shown in several studies (5, 8). Antigenotoxic and chemopreventive effects of this drug was described in several studies (5, 9). It is reported that AV extracts are not fetotoxic and have no abortus effect (10). It is proven that AV gel and extracts increase angiogenesis in chorioallantaoic membrane in chick embryos (11).

Lower protein and soy protein diets are the focal point of medical nutrition therapy for renal health. Recent research indicates that even a moderate incorporation of soy protein into the diet may have significant renal benefits for those at risk for kidney problems (12). Soy protein clearly exerts different effects on renal function parameters compared with animal protein. These effects may be related to one or more of these: isoflavones; amino acid profile; lipid-lowering effects; antioxidant properties; and anti-inflammatory effects (13, 14). Therefore, soy may be beneficial for treatment as well as prevention in persons with kidney problems or in healthy persons at risk of kidney problems (15). High fat diets increased renal inflammation in rats fed cottonseed oil diets, however reduced inflammation in those fed soybean oil and menhaden oil diets (16). Animals fed soy protein had 28% lower relative kidney weights, 37% lower cyst scores and 25% less kidney water (17).

Possible healing effects of AB on the kidneys of rats, which had soybean oil for 3 weeks, were investigated in the present study.

Materials and Methods

The experiments were conducted in compliance with the guidelines for the care and use of laboratory animals approved by Karaelmas University. Wistar Albino rats (n=18; female; three weeks old; weight: 177.51±18.7 g) were equally divided into the one of three groups (control group, experimental group and vehicle group). In experimental group, AB at a doses of 140 mg/kg/day was dissolved in soybean oil and administered as 500 mg capsule form. Soybean oil (500 mg/day) was administrated to the vehicle group. All administrations were given orally by gavage between 10.00-11.00 am for three weeks. All animals were acclimatized to standard laboratory conditions (12 h/12 h light/dark cycle, temperature 23±2 ºC; humidity 40%) and were fed with the same kind of water and special feed.

At the end of the 3rd week, biopsy materials were taken from the right kidneys of all animals. The specimens were fixed in 10% formaldehyde and then processed for light microscopic observations. They were dehydrated in a rising alcohol series processed in xylene and and finally, embedded in paraffin. Sections from paraffin blocks, each approximately 5 thick, were stained with hematoxylin-eosin. Selected areas from all sections were photographed at different magnification (X40, X100, X200, X400).

Results

The results of the light microscopic examinations for control and experiment groups were as follows:

Control group.

An examination of the biopsy materials from the renal cortical areas of the control group animals revealed normal structural features. Malpighi corpuscles were at normal size and structure (Figure 1a). Their diameters were similar. One-fold, flat epithelial cells forming the parietal leaf of Bowman capsule, endothelial and mesenchymal cells in the glomerulus, and podocytes had a normal appearance (Figure 1).The outer leaf of the Bowman capsule, which consists of one-fold flat epithelium, continued with proximal tubular epithelium at the urine pole (Figure 1a). Pyramidal-shaped proximal tubular cells with indefinite lateral boundaries around a narrow lumen were observed. Distal tubules with definite lateral boundaries, which were formed of cells with nuclei in the middle, around a broad lumen were detected at different magnification (Figure 1a). Kidney medulla of the control group revealed normal size and structure (Figure 1b).

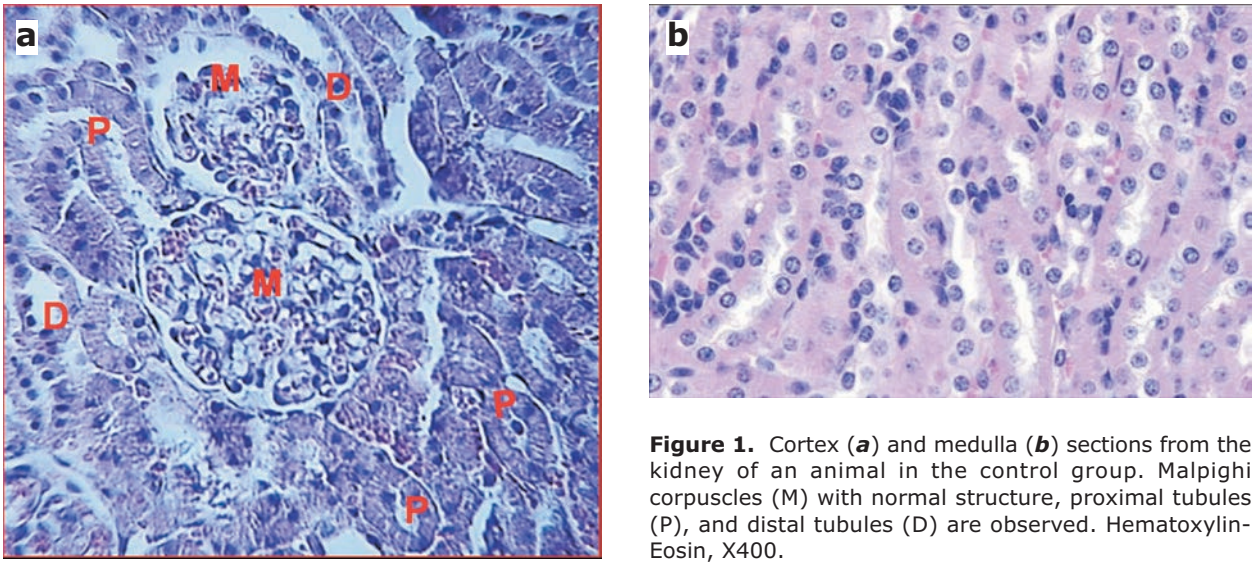


Figure 1. Cortex (***a***) and medulla (***b***) sections from the kidney of an animal in the control group. Malpighi corpuscles (M) with normal structure, proximal tubules (P), and distal tubules (D) are observed. Hematoxylin-Eosin, X400.

Experimental group.

In the examination of all sections from the Aloe Vera administered animals, no marked difference was observed in the Malpighi corpuscles at the light microscopic level (Figure 2).

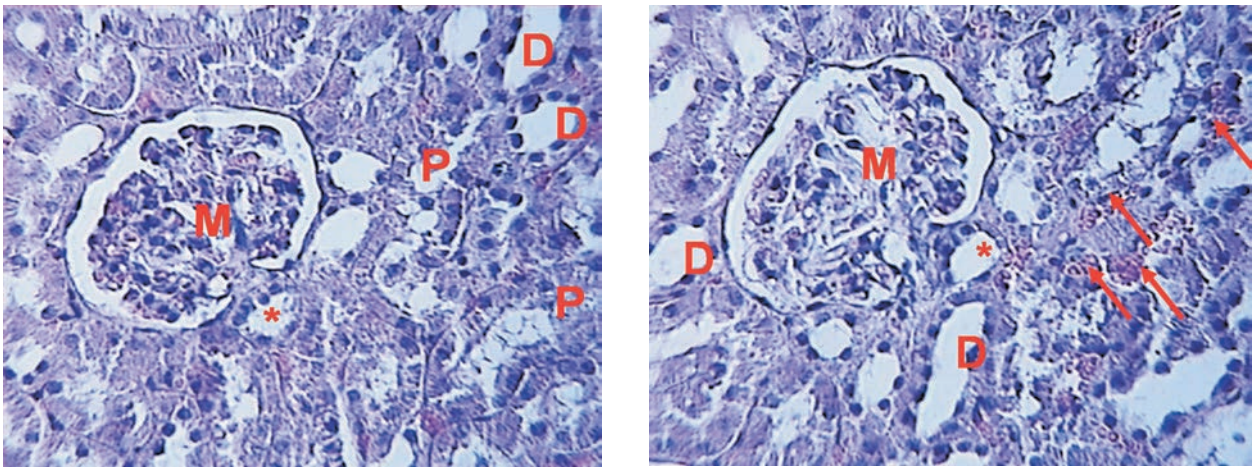


Figure 2. The Malpighi corpuscles (M), distal tubules (D), and macula densa (*) with normal appearance in the sections from the two Aloe-Vera-administered animals. Sporadic cytoplasmic degeneration and vacuolization in proximal tubular cells (P) is striking. Furthermore, congestion (arrow) is observed in the interstitial region. Hematoxylin-Eosin, X400.

Vacuolization with varying degrees in proximal tubules in the cytoplasm and proximal tubular sections was significant. This caused a significant change at their structural characteristics in different areas (Figure 3). Corruption of microvillus formation and cellular desquamation were also seen in some areas. Vacuolization was rare in distal tubules (Figure 3a). Congestion was observed in the cortex in the interstitial region.

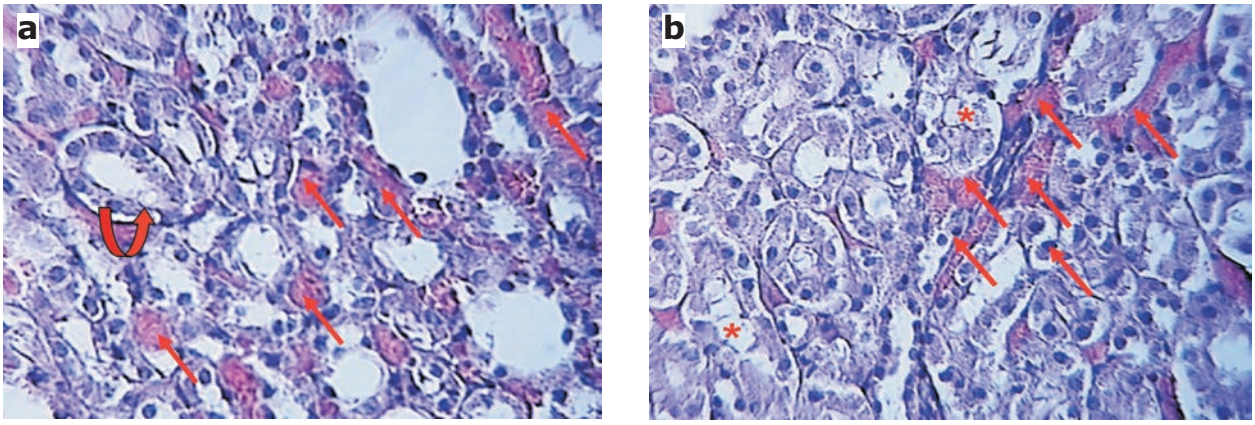


Figure 3. In the sections from the two Aloe-Vera-administered animals, it was observed that the cytoplasm of proximal tubular cells sporadically lost their normal structures, which resulted in vacuolization (*). In Figure 3a, a tubule in which vacuolization has begun among the distal tubular cells with normal structure is marked with a curved arrow. In the marked tubule in the upper-right corner of Figure 3b, a tubule is observed with a completely degenerated structure since it was highly affected by vacuolization. Again, in Figure 3b, there are numerous tubules in which the same kind of degeneration is observed with varying degrees. Moreover, the congestion (arrow) in the interstitial region is another significant finding observed in all the subjects. Hematoxylin-Eosin, X400.

No changes were observed at the microscopic level in the medulla in tubular structures besides some regions which also had congestion (Figure 4).

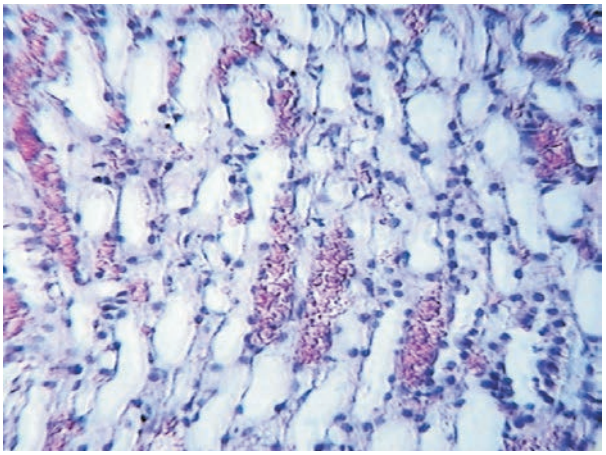
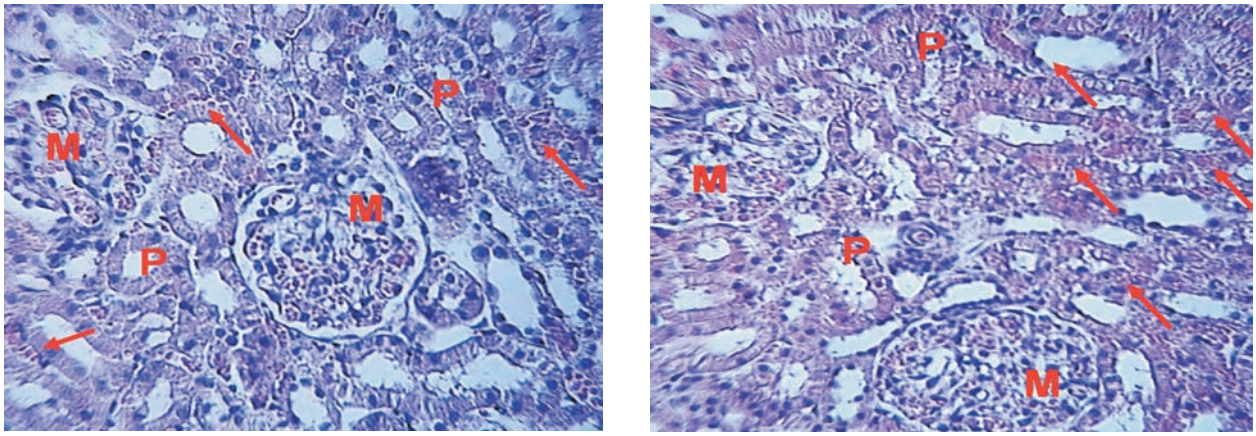


Figure 4. Following the administration of Aloe Vera, congestion is observed in the medulla of the kidney. Hematoxylin-Eosin, X400.

Vehicle group

The kidneys of this group of animals had soybean oil, a solvent for Aloe Vera. Examination of Malpighi corpuscles revealed marked congestion in all glomeruli (Figure 5). Mesangial cellular proliferation was another microscopic common finding in this group. Congestion was also present in the interstitial region (Figure 6). The changes in the proximal tubules were more intense. More proximal tubules with these morphologic changes were observed when compared with the changes in Group II (Figure 6). Vacuolization in distal tubular cells was clear in some areas. Congestive areas were more common in the medulla (Figure 7).



Figures 5. In the sections of two soybean-administered animals, an examination of Malpighi corpuscles (M) reveals marked congestion in the glomerulus. Congestion (arrow) is present in the interstitial region as well. In the proximal tubules, sporadic outpouring and vacuolization (P) are observed. Hematoxylin-Eosin, X400.

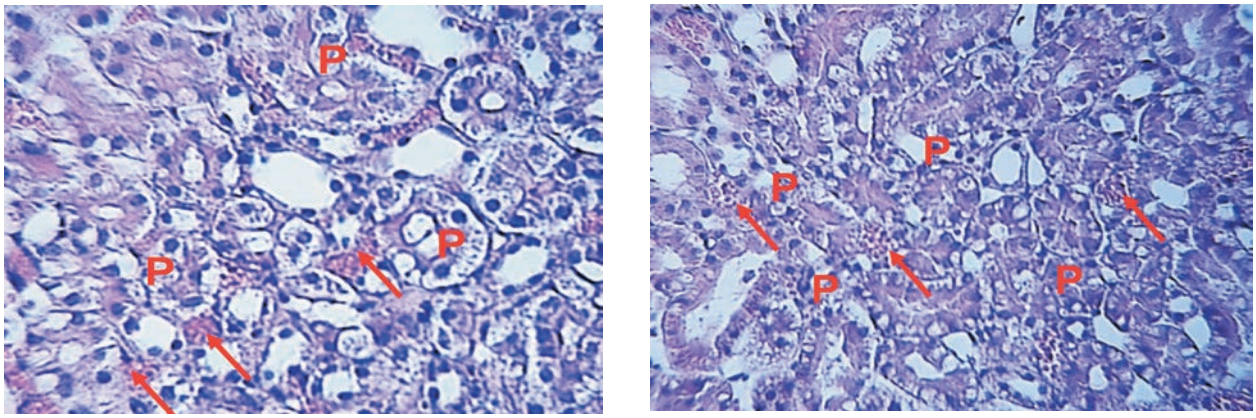


Figure 6. In the sections of two soybean-administered animals, interstitial congestion (arrow), as well as sporadic outpourings and vacuolization (P), are observed in the cytoplasm of proximal tubular cells. Hematoxylin-Eosin, X400.

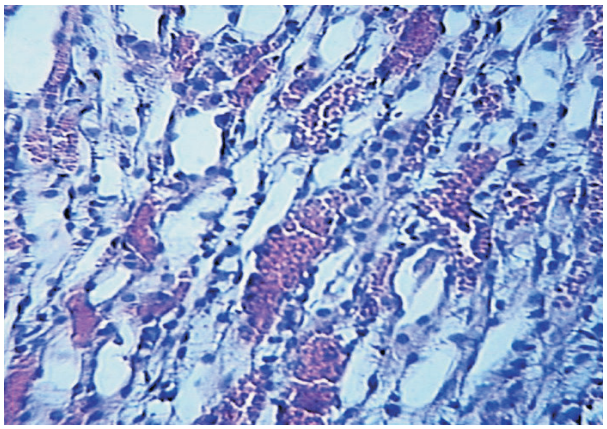


Figure 7. In a soybean-administered subject, congestion is observed in the kidney medulla. Hematoxylin-Eosin, X400.

Microscopic findings were summarized and classified according to the groups and also to the different parts of kidney in Table I.

Table I. Comparison of Light Microscopic Changes on Kidney After Administration of Aloe Vera or Soybean Oil Alone.

	MALPIGHI CORPUSCLES	PROXIMAL TUBULES	DISTAL TUBULES	INTERSTITIUM	MEDULLA
GROUP I	Normal	Normal	Normal	Normal	Normal
GROUP II	Normal	Vacuolisation	Vacuolisation	Congestion	Congestion
GROUP III	Congestion	Increased Vacuolisation	Vacuolisation	Congestion	Increased Congestion

Discussion

There are recent studies investigating the effects of Aloe Vera extracts on different tissues and organs. In a study dried forms of Aloe Barbadensis were treated with petrol, chloroform, methanol and distilled water; then all extracts were tried on mice in which experimental hepatotoxicity was formed with carbon tetrachloride to assess their liver-protecting activity. Best result was obtained with AB treated with distilled water (18). In streptozotocin-induced diabetic rats the ethanolic extract of AV gel was concluded to be used as an antidiabetic agent (19). However there are limited studies investigating the effects of AV extracts on the kidney. Effects of the ethanolic extract of AV gel on membrane-related phosphatase and lysosomal hidrolase in the livers and kidneys of rats with streptozotocin-induced diabetes were investigated in another study. They observed that the enzyme activities were close to normal in diabetic rats to which 300 mg/kg AV extract was orally administered for 21 days. This study has demonstrated that the extract of AV gel has a striking positive effect on membrane-related phosphatase and lysosomal hidrolase (20).

Limited studies were conducted to search the effect of soybean oil on kidney. In a study conducted on rats the effect of different oils on blood pressure and glomerular protection was examined. They examined the renal cortex under light microscope and stereomicroscope and found that the findings of increased blood pressure, glomerulosclerosis, enlargement and loss of glomeruli in hypertensive rats were prevented in the group fed with fish, canola and palm oils, while they showed regression in the group fed with olive oil and soybean oil. Yet, the weakest protection effect was observed in soybean oil (21). In another study the effect of nutritional oils in daunomycin-induced nephropathic mice was investigated. A comparison was made between fish oil and soybean oil. In the group fed with fish oil, a significant decrease in urinary albumin excretion and improvement in daunomycin-induced histological changes were observed. On the other hand, tissue lipid peroxidase levels, which increased in the group fed with soybean oil, were suppressed in the mice fed with fish oil. Renal tissue GSH peroxidase activity was significantly lower after 72 hours following daunomycin injection 6edin the group fed with fish oil than that fed with soybean oil. Renal cortical TxB2 and 6-keto prostaglandin F1 alpha levels were significantly lower in the group fed with fish oil when compared to the other group fed with soybean oil. These results allowed the researchers to maintain that inhibition of oxidative damage through nourishment with fish oil had a crucial role in preventing daunomycin-induced nephropathy in mice model (22).

The above-mentioned studies investigated the effect of either AV or soybean oil on the kidney, however, in the present study, we used both AB and soybean oil groups. We observed similar results in the both groups. However, these changes were more expansive and intense in the group only fed with soybean oil. Congestion in the glomeruli was detected only in the group fed with soybean oil. We observed healing effects of AB on nephrotoxicity induced by soybean oil in rats. Our results correlate with the findings of previous authors.

The above results suggest that AB has a possible therapeutic effect by eliminating the toxic effects of soybean oil on the kidney (particularly in Malpighi corpuscles).

These findings at the light microscopic level must be supported by electron microscopic, immunohistochemical and histomorphometric examinations. The next step of these studies is to determine the cellular mechanism(s) of these effects of this agent.

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