Department of Pharmacology[1], Faculty of Medicine, Atatürk University, Erzurum,Turkey and Department of Pharmacognosy[2], Faculty of Pharmacy, Hacettepe University, Ankara,Turkey

Effect of the aqueous extract of *Rumex patientia* on xylol and hyaluronidase induced capillary permeability compared to indomethacin

H. Süleyman[1], L. Ö. Demirezer[2], A. Kuruüzüm[2], M. E. Büyükokuroğlu[1], F. Göçer[1], Z. N. Banoğlu[1] and A. Gepdiremen[1]

In this study, the effect of an aqueous extract of *Rumex patientia* L. (Polygonaceae) (D-1) on capillary permeability which was induced by xylol and hyaluronidase was investigated. Experiments were conducted on rabbits according to Monakova and Matusis methods. The effects of D-1 were compared to those of indomethacin, which was used as a control throughout the experiment. Both D-1 (100 mg/kg) and indomethacin (10 mg/kg) were administered orally. As a result, D-1 inhibited capillary permeability, which was induced by xylol and hyaluronidase, and it was found that it was as effective as indomethacin.

1. Introduction

Rumex patientia L., a member of the Polygonaceae family, is a ca. 2 m tall herb which is widely distributed in Turkey at an altitude of ca. 1050 m. [1]. This plant contains anthraquinones, naphthalenes and tannins as major components [2]. The roots of *R. patientia* have been used extensively in traditional medicine in Turkey as a laxative, diuretic, antipyretic, wound healer and as an antiinflammatory agent [3]. It has been reported that aloin and rhein, two anthraquinones, exhibit antiinflammatory effects [4, 5]. Additionally, condensed tannins are mainly responsible [6] for the antiphlogistic and immunostimulating effects of *R. acetosa*, which is used in acute and chronic sinusitis in combination with other herbal drugs. Inflammation mediators, which are histamine, serotonine, prostaglandine (PGE_1, PGE_2) and bradykinin, play an important role during the generation of inflammation [7, 8]. These mediators cause an increased capillary permeability, and depending on this, an exudation gathering in tissues [9]. Hyaluronidase activity in blood is increased during inflammation [10]. In our previous study, D-1 was effective in histamine-, formaldehyde-, dextrane-, serotonine- and carrageenan-induced inflammation models. D-1 also decreased the inflammation in adrenalectomized rats [11]. During the occurrence of inflammation, not only inflammation mediators, but also vascular permeability plays an important role [12]. Indomethacin shows its antiinflammatory activity by inhibiting the synthesis of inflammation mediators and decreasing capillary permeability [13]. In this study, the effects of a nonsteroidal antiinflammatory drug (NSAID), indomethacin, and D-1 on increasing capillary permeability induced by xylol and hyaluronidase were compared according to the Monakova [14] and Matusis [15] methods.

2. Investigations, results and discussion

As it is known, antiinflammatory drugs inhibit exudation gathering [16] by decreasing capillary permeability in inflamed area [17, 18]. NSAIDs decrease vascular permeability by inhibiting the biogenic amines [19]. Xylol causes local inflammation in skin and increase capillary permeability [20–22]. Neuropeptides play important roles in the pathogenesis of xylol-induced inflammation [21]. As it is seen in Table 1, the time to appearance of tripan blue after xylol addition was 2.8 ± 0.49 min in control animals. This period was 4.9 ± 0.55 min for D-1-administered animals while in indomethacin treated animals, it was 4.6 ± 0.36 min. According to Monakova [14], there is a linear correlation between the time to appearance of the blue colour and capillary dilation and inflammation; the shorter the appearance time, the greater the capillary dilation and inflammation. It is evident from the data that D-1 is as effective on xylol-induced capillary permeability as indomethacin. The time difference between the appearance period in the control group and the D-1-administered group was 2.1 min, whereas the time difference between the appearance period in the control and indomethacin-administered group was 1.8 min. The difference between D-1 and indomethacin was only 0.3 min. Similar results were obtained in hyaluronidase-induced capillary permeability studies. Hyaluronidase hydrolizes hyaluronic acid in tissue and causes increased tissue permeability [23, 24]. As it is shown in Table 2, the subcutaneous spreading area of tripan blue administered together with the hyaluronidase enzyme was 151.6 ± 7.27 mm^2 in the control group, 100.9 ± 7.57 mm^2 in the D-1 treated group and 119.2 ± 7.11 mm^2 in the indomethacin treated group. According to Matusis [15], smaller blue areas indicated a decrease in hyaluronidase enzyme activity and capillary permeability, whereas larger blue areas indicated the opposite. In the control group, the spreading area caused by hyaluronidase was 50.7 mm^2 larger than that of D-1 and 32.4 mm^2 larger than that of indomethacin. It is clear from this data that hyaluronidase caused more vascular dilation in the control group than in the other two groups. These

Table 1: Effect of D-1 and indomethacin on xylol induced capillary permeability

Samples	Dosis (mg/kg)	Appearence of Colours (min)	P
D-1	100	4.92 ± 0.55	< 0.05
Indomethacin	10	4.62 ± 0.36	< 0.05
Control	–	2.83 ± 0.49	–

Table 2: Effect of D-1 and indomethacin on hyaluronidase induced capillary permeability

Samples	Dosis (mg/kg)	Spread area of hyaluronidase (mm^2)	P
D-1	100	100.9 ± 7.57	< 0.001
Indomethacin	10	119.2 ± 7.11	< 0.01
Control	–	151.6 ± 7.27	–

results show that capillary permeability is significantly decreased by D-1. Moreover, D-1 when administered in a dose of 100 mg/kg, decreased capillary permeability by the same order of magnitude as indomethacin.

In conclusion, our research proved that D-1 is effective in serotonine-, histamine-, formaldehyde-, dextrane-, xylol- and hyaluronidase-induced inflammation models, and that its antiinflammatory activity was as good as that of indomethacin. Our previous research [11] showed that the antiinflammatory activity of D-1 was not dependent on glucocorticoids. However, detailed studies are needed to determine the mechanism of D-1 activity.

3. Experimental

3.1. Plant material

The roots of *R. patientia* L. were collected from Niğde-Bor (1050 m) in September 1994. The plant was identified by Dr. L. Korkmaz of the Department of Botany of Ankara University, Turkey. Voucher specimens are deposited in the herbarium of the Faculty of Pharmacy, Hacettepe University (HUEF-94102) Ankara.

3.2. Extraction and preparation of the test samples

The material (5 g) was exhaustively extracted in a Soxhlet apparatus with water at 40 °C and the extract was liyophilized. The extract (D-1) yield was 1.2 g (24%).

3.3. Animals

In this study 36 albino rabbits, weighing 3–3.5 kg and nourished under the normal conditions at the Atatürk University, Experimental Animal Laboratory, Erzurum, were used.

3.4. Method of Monakova [14]

The effect of D-1 was investigated on xylol induced capillary permeability. For this study, 18 albino rabbits, weighing 3–3.5 kg, were used. The animals were divided into three groups (n = 6/group). The first group of rabbits received 100 mg/kg of D-1, and the second group 10 mg/kg of indomethacin, and the control group received saline solution orally. After 1 h, 1 ml/kg of tripan blue (1%) was injected to the ear venous of all the animals. Five minutes after injection, 0.02 ml xylol was spotted dropwise on the shaved abdominal areas of each animal, and time until appearence of blue colour was determined.

3.5. Method of Matusis [15]

The activity of D-1 was investigated on hyaluronidase-induced capillary permeability. For this study, 18 albino rabbits, weighing 3–3.5 kg, were used. The animals were divided into three groups (n = 6/group). The doses of D-1 and indomethacin mentioned above (3.4.) were administered. 128 IU hyaluronidase was dissolved in 1 ml saline solution, and 0.5 ml of this solution was added to 0.8 ml tripan blue solution (0.75%). After 1 h, 0.1 ml of this solution was subcutaneously injected to the shaved area of each animal. After 20 s, blue areas were measured in mm^2.

3.6. Acute toxicity

In a previous study acute toxicity of D-1 was tested. From 500 to 3000 mg/kg doses of D-1 were administered to rats (p.o). None of the rats died [11].

3.7. Statistical methods

Values reported are mean ± SEM. Student's t test and a probability level of $p < 0.05$ were chosen as the criterion of statistical significance.

References

1 Davis, P. H.: Flora of Turkey and east Aegean Islands, vol. 2, p. 281, University press, Edinburgh 1965
2 Demirezer, L. Ö.; Kuruüzüm, A.: FABAD, J. Pharm. Sci. **22**, 153 (1997)
3 Baytop, T.: Türkiye'de Bitkiler ile Tedavi, p. 314, Sanal matbaaclk, İstanbul 1984
4 Yamamoto, M.; Masui, T.; Suglyama, K.; Yokota, M.; Nakagomi, K.; Nakazawa, H.: Agricul. Biol. Chem. **55**, 1627 (1991)
5 Mian, M.; Benetti, D.; Rosini, S.; Fantozi, R.: Int. J. Tissue Reaction **11**, 117 (1989)
6 Schwartner, C.; Wagner, H.; Christoffel, V.: Chemical and Pharmacological Investigations on *Rumex acetosa* L. Second International Congress on Phytomedicine Abstracts, Supplement I, Munich, Germany, 11–14 September. 1996
7 Sigidin, Y. A.; Schwarz, G. Y.; Arzamaszev, A. P.; Liberman S. S.: M. Medicina, 240 (1988)
8 Chensue, S. W.; Ward, R. A.; in: Damjnow, I., Linder, J., (eds). Anderson's pathology, Tenth edition, p. 387–415, Missouri Mosby-Year Book Inc, 1996
9 Oyvin, I. A.; Gaponyuk, P. Y.; Oyvin V. I.: Potol Fiziol i Eksperim. Ter. **4**, 19 (1972)
10 Ginzburg, P. M.: Braçep Delo **9**, 23 (1962)
11 Süleyman, H.; Demirezer, L. Ö.; Kuruüzüm, A.; Banoğlu, Z. N.; Göçer, F.; Özbakış, G.; Gepdiremen, A.: J. Ethnopharmacol. **65**, 141 (1999)
12 Martin, G.; Southwell, W.: Expt. Med. Surg. **23**, 150 (1965)
13 Insel, A.; In: Gilman, A. G. (ed) Godman and Gilman's the Pharmacological basis of therapeutics, p. 617, Mc Graw-Hill, New-York 1996
14 Monakova, K. H.: Tadj Med Inta Duşanbe **1**, 27 (1954)
15 Matusis, I.: Farmakol i toksikol M. **13**, 9 (1950)
16 Schwarz, G. Y.; Syubayer, R. D.: Farmakol i Toksikol. **1**, 46 (1982)
17 Guobis, G.; Yuşşinayte, Y.: Terapevt Arh. **7**, 142 (1981)
18 Trinus, F. P.: Farmako-terapevtiçeskiy spravoçnik şestoye izdaniye, p. 331, Kiev Zdorovya 1988
19 Wilhelm, G.: Schweiz. Med. Wschr. **8**, 936 (1950)
20 Saratikov, A. S.; Prishchep, T. P.; Yavorowskaya, V. E.: Izd-vo Tomsk un-ta, 198. (1975)
21 Iyadomi, M.; Higaki, Y.; Ichiba, M.; Moromoto, M.; Tomokuni, K.: Ind. Health **36**, 40 (1998)
22 De La Puerta, R.; Martinez, E.; Bravo, L.; Ahumada, M. C.: J. Pharm. Pharmacol. **48**, 268 (1996)
23 Trinus, F. P.; Mohort, N. A.: Farmakol. i toksikol. M. **1**, 60 (1972)
24 Smith, E. L.; Hill, R. L.; Lehman, I. R.; Lefkowitz, R. J.; Handler, P.; White, A.: Principles of biochemistry (mammalian biochemistry). Koon Wah Printing Ptc Ltd, Singapore 1983

Received January 10, 2000
Accepted May 5, 2000

Assoc. Prof. Dr.
L. Ömür Demirezer
Department of Pharmacognosy
Faculty of Pharmacy
Hacettepe University
06100-Sıhhiye
Ankara
Turkey
omurd@hacettepe.edu.tr