J. Black Sea/Mediterranean Environment
Vol 10: 201 - 208

Prostaglandin in Algae
Investigation on *Halopteris filicina* (Kütz.) Extract

Alglerde Prostaglandin
Halopteris filicina (Kütz.) Ekstresinde

K.C. Güven[1], Z. Kızıl[1], O. Özdemir[2], G. Kaya[3], O. N. Ulutin[3], R. K. Türker[4]

[1] Department of Pharmaceutical Techonology,
[2] Department of Pharmacology, Faculty of Pharmacy, University of Istanbul.
[3] Hemostasis and Thrombosis Research Center, Cerrahpaşa Medical Faculty, University of Istanbul.
[4] Department of Pharmacology, Faculty of Medicine, University of Ankara, Turkey.

Abstract

In this work the prostaglandin – like activity was investigated in extract of *Halopteris filicina* (Kütz.). The methods used for examination of prostaglandin activity of the algal extract were; ADP, adrenaline and collagen induced aggregation in human platelet rich plasma. The results showed that *H. filicina* extract, depending on this concentration, inhibited the secondary waves of platelet aggregation induced by ADP and adrenaline and also aggregation waves induced by collagen.

Thus it was demonstrated that the algal extract inhibited the secretion of the platelets and mild inhibitory effect was seen on the primary waves. These data showed the indication of PGE_1 – like activity in *H. filicina.*

This paper is the repeated article on the prostaglandin activity of red algae *Halopitis filicina* which was the second report in the literature on prostaglandin activity of algae when published in Acta Pharma Turc. (Güven *et al.*, 1984).

Key words: *Halopteris filicina*, prostaglandin E_1

Introduction

Prostaglandin was found in extracts from human prostate. It is widely distributed in various organs, and exhibits various biologically important activities such as smooth muscle dilatation/ contraction, body temperature regulation, induction of pain stimulation of bone resorption and inhibition of immune responses (Watanabe *et al.*, 2003).

Prostaglandin are all derived from 20 carbon polyunsaturated fatty acids and are collectively termed eicosanoids. In man the most common precursor is arachidonic acid (eicosatetraenoic acid). Another definition is that prostaglandins are derivatives of the carbon skeleton 7 –(2 – octyl cyclopentyl) heptanoic acid (also known as prostanoic acid). There are many types of prostaglandings as E_1, E_2, E_3 and F_{1a}, F_{2a}, F_{3a}.

Isoprostanes are products of free radical- catalysed oxidation of arachidonic acid (20:4) in mammals.

In earlier studies on *Halopytis sp.* are found 3- bromo – 4,5 dihydroxy benzaldehyde (Wagner *et al.*, 1981); succinic acid, stearic acid, sterol, agar, Vit. B_{12} from *H. incurvus* (Güven and Kızıl, 1986).

Novel prostaglandins in animals and plants: the isoprostanes were investigated by Mueller (1998). In the algae studies were: The prostaglandins PGE_2 and $PGE_{2\alpha}$ were isolated first from algae. *Gracilaria lichenoides* (Greason *et al.*, 1979) and PGE_1 from *Halopteris filicina* (Güven *et al.*, 1984), PGE_2 from *Gracilaria verrucosa* (Fusetani and Hashimoto, 1984), 15 keto PGE_2 from *G. asiatica* (Sajiki, 1999) (Sajiki and Kakimi, 1998).

The influence of environmental factors on prostaglandin content of *G. verrucosa* was also investigated (Imbs *et al.*, 2001).

The biochemical pathway of the formation of phytoprostanes is analogous to the isoprostane pathway in mamals. Oxidation and cyclization of α – linolenic acid yield two regioisomeric phytoprostane G_1 (type I and III). Phytoprostanes G1 are unstable molecules that readily decompose to phytoprostanes D_1, E_1 and F_1 (Loeffler *et al.,* 2003). PGF_2 in *G. verrucosa* (Sajiki and Kakimi 1998; Sajiki, 1999). PGA_2, PGE_2, PGF_2 and 15 PG_2in *G. verrucosa* (Imbs, 2001).

The aim of this paper is to bring to the attention of the workers on prostaglandin that the article published in Acta Pharmaceutica Turcica, 1984 on the prostaglandin activity of *Halopiteris filicina* has not been referred by any abstract.

This paper is the repeated article on the prostaglandin activity of red algae *Halopitis filicina* which was the second report in the literature on prostaglandin activity of algae when published in Acta Pharma Turc. (Güven *et al.,* 1984).

Material and Method

Halopteris filicina (Kütz.) was collected at Zeytin alanı, İzmir in 1982 and 1984.

The fresh material was washed with distilled water then with acetone to remove water residue on the surface of algae. It was cut into small pieces and extracted with ethyl acetate. The extract was distilled under vacuum.

PG- like activity was determined by bio assay technique (Vane, 1983) based upon the response of the isolated rat stomach fundus strip bathed in a warmed (37 °C) and oxygenated (5 % CO_2 in O_2) Krebs-Henseleit solution. 1.0 g initial tension was applied and the isometric contractions of the strips were recorded on a Grass polygraph (Model 79 D9 via-force displacement trandsducers (Grass FT. 03). The antagonists such as atropine (0.1 μg/ml), methysergide (1 μg/ml), mepyramine (0.1 μg/ml)and phentolamine

(2 μg/ml) were added to the incubation medium in order to eliminate possible interference of acetycholine, serotonin, histamine and noradrenaline on muscle response.

After testing the concentration-response curve of standard PGE_1, 0.1 ml algal extract was added to the bath and the response was recorded. In addition, the effect of algal extract on platelet aggregation was also tested in vitro in human platelet rich plasma by Born and Cross method (1963).

ADP, adrenaline and collagen induced aggregations were determined by using Briston Aggregometer and Bausch and Lomb recorder (Ulutin, 1976).The final concentration of ADP and adrenaline were 0.5 and 1.0 μg/ml. Collagen concentration was 5 μg/ml. The following mixture was used:

0.4 ml PRP (platelet rich plasma), 0.05 ml solution of algal extract in different concentrations and 0.05 ml solution of aggregating agents. The curves were recorded.

Results and Discussion

The algal extract produced a concentration in the rat stomach fundus strip which was not inhibited by atropine, mepyramine, methysergide and phentolamine. This indicated that the extract had not contained cholinergic, histaminergic and serotoninergic activities (Fig. 1). The contractile effect of the extract, however, could be blocked by SC 19220 at concentrations between 10^{-6} and 10^{-5} M which was a competitive receptor blocker of PGs in smooth muscle preparations (Sanner, 1969). In addition, the algal extract also caused an inhibition on ADP, adrenaline and collagen induced aggregation in human platelet rich plasma (Fig. 1-3). This finding supported the assumption that PG-like activity in this extract should be one of PGs series (Probably PGE_1), since two series of PGs, especially $PGE_{2\alpha}$ were described as strong aggregatory agents on platelet rich plasma. The total amount of PGE_1- like activity of extract obtained from 1300 g *H. filicina* was found to be equal to 200 ng PGE_1.

The data showed indicate the presence of PGE_1- like compound in marine algae *H. filicina* extracts.

The first paper on prostaglandin activity of algae was published by Greason *et al.*, 1979 and this finding is the second observation of prostaglandin activity in algae (Güven *et al.*, 1984).

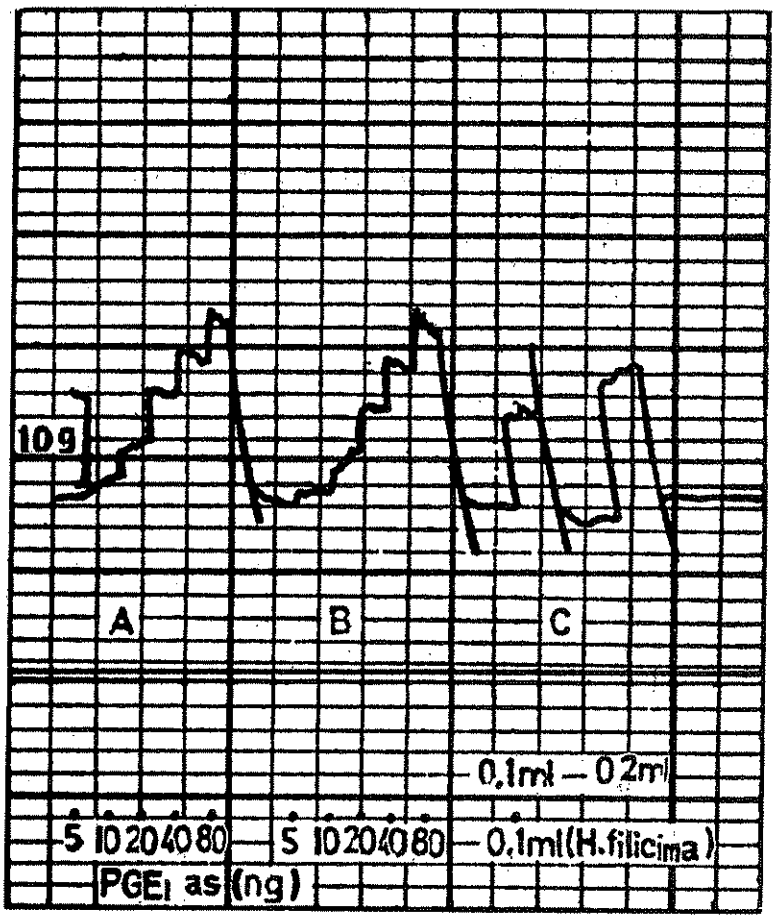

Fig.1 **ADP induced aggregation; 0.4 ml PRP + 0.05 ml ADP + 0.05 ml saline (A), Algal extract solution (corresponding to 500 g fresh alga) dilution: x 30 (B), x 60 (C), x 120 (D), x 240 (E), x 480 (F).**

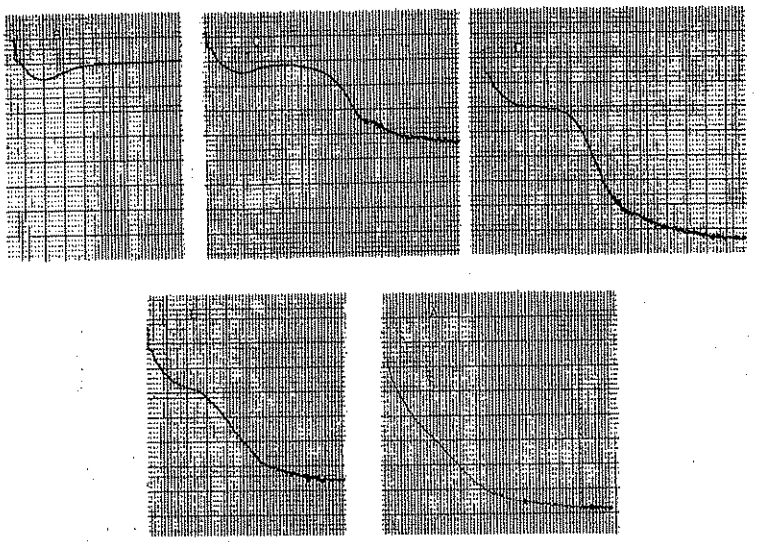

Fig. 2 ADP induced aggregation; 0.4 ml PRP + 0.05 ml ADP + 0.05 ml control saline (A), Algal extract solution (corresponding to 500 g fresh alga) dilution: x 30 (B), x 60 (C), x 120 (D), x 240 (E), x 480 (F)

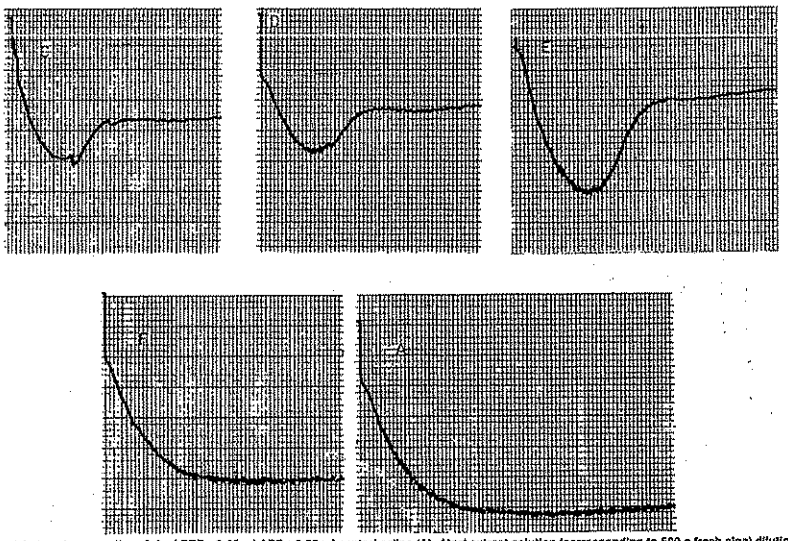

Fig. 3 ADP induced aggregation; 0.4 ml PRP + 0.05 ml ADP + 0.05 ml control saline (A), Algal extract solution (corresponding to 500 g fresh alga) dilution: x 30 (B), x 60 (C), x 120 (D), x 240 (E), x 480 (F)

References

Born, G.V.R., Cross, M.J. (1963). Aggregation of blood platelett. Br.J. Physiol. (London) 168: 178.

Fusetani, N. and Hashimoto, K. (1984). Prostaglandin E_2 – a candidate for causative agent of ogonori poisoning. II. *Bull. Jpn. Soc. Sci.* 50: 465-469.

Greason, R. Marwood, F. and Quinn, R.J. (1979). The occurence of prostaglandins PGE_2 and $PGF_{2\alpha}$ in a plant- red alga *Gracilaria lichenoides*. *Tetrahedson Letters* 46: 4505 – 4506.

Güven, K.C., Kızıl, Z., Özdemir, O., Kaya, G., Ulutin, O.N., Türker, R.K. (1985). Prostaglandin – like activity of *Halopteris filicina* (Kutz) (Marine alga) extract. *Acta Pharmaceutica Turcica* 27: 92 – 95.

Güven, K. C, Kızıl, Z. (1986). Chemical studies on *Haoplytys incurvus* (Huds.) batters (Rhodophyceae). Acta pharmaceutica Turcica 28: 11 – 15.

Imbs, A.B., Vologodskaya, V., Nevshupova, N.V., Khotimchenko, S.V., Titlyanov, E.A. (2001). Response of prostaglandin content in the red alga *Gracilaria verrucosa* to season and solar irradiance. *Phytochemistry* 58: 1067-1072.

Loeffer, C., Thoma, I., Krische, M. and Mueller, M.J. (2003). The dinor isoprostane pathway in plants. In: Advance in prostaglandin, Leukotrien and other bioactive lipid usearch (Z. Yazıcı, G.C. Folco, J.M. Drazen, S. Nigam and T. Shimizu, eds.) Kulver Academic/ Plenum Publishers, New York, 2003.

Mueller, M.J. (1998). Radically novel prostaglandins in animal and plants: the isoprostanes. *Chem. Biol.* 5: 323-333.

Sajiki, J. (1999). Acid treatment increased leucotriene B_4 in the red alga *Gracilaria asiatica* (= verrucosa). *Fisheries Sci.* 65: 914-918.

Sajiki, J. and Kakimi, H. (1998). Identification of eicosanoids in red alga *Gracilaria asiatica* using high performance liquid chromatography and electro assay ionisation mass spectrometry. *J. Chromatogr.* 795: 225-237.

Sanner, J.H. (1969). Antagonism of prostaglandin E2 by 1- acetyl- 2- 8 – Chloro- 10,11 dihydrobenz (b,f) (1.4 oxazepine –10 carbonyl) hydrozine (SC. 19220). *Arch. Int. Pharmacodyn* 180: 46.

Ulutin, O.N. (1976). The platelets, Fundamental and Clinical Applications, Kağıt Basım İşleri, A.Ş., İstanbul.

Vane, J.R. (1983). Adventure and excussions in bioassay: the stepping stones to prostacyclin. *Br. J. Pharmacol.* 79: 821.

Wagner, M., Güven, K.C., Kızıl, Z., Vural, S., Öğütman, R. (1981). A bromo compound in *Halopytis incurvus* (Huds.) Batters. Vie et Milieu 31:15 –16.

Watanabe, K., Ohmiya, O., Ohkubo, H., Tanikawa, N. Kojima, M and Seiji, I. (2003). A novel type of membrane- associated prostaglandin E synthase. In: Advences in prostaglandin, Leukotrien and other bioactive lipid research (Yazıcı, Z., Folco, G.C., Drazen, J.M., Nigam, S., Chimizu, T. eds.) Kluver Academic/Plenenum Publishers, Newyork pp 107-111.

Received: 05.01.2004
Accepted: 11.02.2004