International Journal of Cell, Animal Biology and Genetics
Vol.6, No.1, pp., 46-54, 2021
Print ISSN: ISSN 2397-8147
Online ISSN: ISSN 2397-8155

HISTOLOGICAL EFFECTS OF AQUEOUS STEM BARK EXTRACT OF *CADABA FARINOSA* ON THE GASTROINTESTINAL TRACT OF ADULT WISTAR RATS

[1]S.M Gamde, [2]M Umar, [3]O.G Avwioro, [4]A.A Muhammad, [2]A.A Musa, [5]E.S Bwede
[1] Department of Pathology. General Hospital Silame. Sokoto. Nigeria
[3] Faculty of Science, Delta State University, Abraka. Nigeria.
Department of [2]Morbid Anatomy and Forensic Medicine, [4]Pharmacology and Toxicology,[5]
Department of Chemical Pathology, Usmanu Danfodiyo University, Sokoto. Nigeria.

ABSTRACT: *In a global context and developing countries Nigeria inclusive, herbal medicines are major source of healt:hcare. Among plants widely used as therapeutic agents for treating various forms of cancer is Cadaba farinosa. However, there are limited published reports about the possible therapeutic effects of this plant especially on the gastrointestinal tract. The aim of this study is to evaluate the effects of aqueous stem bark extract of Cadaba farinosa on the gastrointestinal tract of adult Wistar rats.Thirty adult rats of both sexes were used and divided into five groups of six rats each. Group 1 served as control. Aqueous extracts were administered to study groups (2, 3, 4 and 5) at different doses of 100, 200, 300 and 400 mg/kg respectively. Haematological parameters such as RBC count and RBC indices (Hgb, MCV, MCH and MCHC) determined after 28 days (sub-chronic) using standard techniques. Histology of gastrointestinal tract was examined at highest dose of 400mg/kg. This study showed that acute oral administration of aqueous stem bark extract of Cadaba farinosa is relatively safe up to 5000mg/kg body weight/day. Histological findings showed normal sections of gastrointestinal tract among study groups. However, there are increased goblet cells proliferations and secretions in animals treated with various doses of extract. The haematological parameters were within normal limits.Aqueous stem bark extract of Cadaba farinosa in animal models ameliorates gastrointestinal mucosal damage resulting from reduced mucosal barrier from mucus secretion (anti peptic ulcer).*

KEY WORDS: *Cadaba farinosa*, ulcer, Wistar rats, gastrointestinal tract.

INTRODUCTION

In most developing countries, herbal medicinal plants are introduced into markets without mandatory toxicological evaluations [1]. Consumers of herbal products are without prescriptions in most cases and the potential hazards of inferior products are hardly recognized [2]. As herbal therapies continues to grow and recognized worldwide, the general perceptions that herbal remedies are safe and devoid of adverse effects is not only untrue but also misleading [3, 4 and 5]. Herbs may contain harmful substances especially long term usage [6, 7]. Several literatures have

ECRTD-UK https://www.eajournals.org/
ULR: https://doi.org/10.37745/ijcabg.16

reported some herbs to cause undesirable life's threatening gastro intestinal disorders and splenic enlargement [8] which could result to death [1].

Among plants widely used for therapeutic purposes is *Cadaba farinosa forsk.* The plant belongs to the Capparidaceae family with 45 genera and 600 species, distributed worldwide [9]. Phytoconstituents of *Cadaba farinosa* include Alkaloids, Protein, Flavonoid, Spermidine, Glycoside, Tannins, Quercetin, and Steroids [10, 11, and 12]. In North Eastern Nigeria, *Cadaba farinosa* is used for treating various forms of cancers, female infertility and gastrointestinal parasites [13, 14 and 15]. However, there is paucity of information on its effects on the gastrointestinal tract, a major route in extract administration..

MATERIALS AND METHOD

Study Area
This research was carried out at the General Hospital Silame, Sokoto in collaboration with Department of Histopathology Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria.

Experimental Animals
Thirty (30) male and female Wistar rats (180-200g) were used in this research. Rats were obtained from Animal House, Faculty of Pharmaceutical Science, Usmanu Danfodiyo University Sokoto. The rats were kept in cages, supplied with clean drinking water and fed *ad libitum* with standard commercial feed.

Plant Collection
Inner stem bark of *Cadaba farinosa* was harvested fresh at Faculty of Pharmaceutical Science, Usmanu Danfodiyo University Sokoto. Nigeria. The plant was identified at the Faculty of Pharmaceutical Sciences, Department of Pharmacognosy and Ethno-medicine with voucher number PCG/UDUS/CAPP/0002.

Plant Extraction
The fresh inner stem bark of *Cadaba farinosa* was dried in the laboratory at room temperature and powdered with Pestle and Mortar. 210g of dried powdered plant was macerated in 600mL of water at room temperature for 24 hours. The solution was filtered with Whatmann's filter paper to obtain particle free solution and filtrates evaporated to dryness at 45^0C in water bath as described by [16].

ECRTD-UK https://www.eajournals.org/
ULR: https://doi.org/10.37745/ijcabg.16

Experimental Animals

A total of thirty (30) adult Wistar rats of both sexes were acquired from the Animal House of the Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University Sokoto.Nigeria. The animals were properly fed with standard rat pellets and water.

Experimental Design

Each group of animal was given different doses of extract orally using intra-gastric tube. The method of administration for acute toxicity study and LD_{50} determination was according to Lorkes [17]. The extracts were administered once and observed closely for 24 hours. For sub-chronic toxicity study, experimental animals received aqueous extract of *Cadaba farinosa,* while control group were given water daily for consecutive 4 weeks. Route of administration was intra-gastric using a ball-tipped stainless steel feeding needle fitted to a 5ml syringe.

Laboratory Examination

At the end of intervention, animals were sacrificed using chloroform. Blood was culled by cardiac puncture using 5ml sterile plastic syringes and needles from each subject aseptically; about 2.5ml EDTA anticoagulant bottle for haematological analysis. Tissues were kept in 10% formal saline for 24 hours, processed and stained by H&E as described by Avwioro [18].

Statistical Analysis

Data were entered using Microsoft excel and exported into SPSS version 20. Analysis was done using one way repeated measures analysis of variance (ANOVA). A statistically significant differences among the groups presented as mean ±SD. Values of $P \leq 0.005$ were considered significant.

ECRTD-UK https://www.eajournals.org/
ULR: https://doi.org/10.37745/ijcabg.16

RESULT

Table 1: Acute Toxicity of Aqueous Stem Bark Extract of *Cadaba farinosa* in Adult Wistar Rats (N=9).

DOSE	MORTALITY	
	PHASE I	PHASE II
10mg	0/3	-
100mg	0/3	-
1000mg	0/3	-
1600mg	-	0/1
2900mg	-	0/1
5000mg	-	0/1

Table 2: Comparison of Haematological Parameters of Rats treated with Aqueous Stem Bark Extract of *Cadaba farinosa* and Control Group

Doses	RBC (×106/uL)	WBC ×103/uL)	PLT (×103/oL)	HGB (g/dL)	HCT (%)
Control	3.00 ± 0.8	38.30 ± 10.43	1081.67 ± 51.50	10.40 ± 0.17	31.23 ±0.49
100mg/kg	2.47 ± 0.61	26.10 ± 1.57	721.00 ± 178.40	8.60 ± 2.94	25.50 ± 8.59
200mg/kg	2.47 ± 0.61	26.80 ± 1.73	1270.33 ± 567.28	8.60 ± 2.94	25.80 ± 8.83
300mg/kg	3.18 ± 0.00*	19.93 ± 3.88	2128.67±1457.85	10.30 ± 0.00*	30.90 ±0.00*
400mg/kg	2.83 ± 0.61	21.30 ± 2.14	1551.67 ± 184.45	17.17 ± 5.95	51.50 ±17.84

Red Blood Cell (RBC), Haemoglobin (HGB), and Haematocrit (HCT) had a P value of 0.00 which is considered statistically significant. Whereas, White Blood Cell (WBC), and Platelet (PLT), expressed in Mean ± SD used in determining the effects of aqueous extract was not significant on ANOVA with a Greenhouse-Geisser test after administration of extract.

ECRTD-UK https://www.eajournals.org/
ULR: https://doi.org/10.37745/ijcabg.16

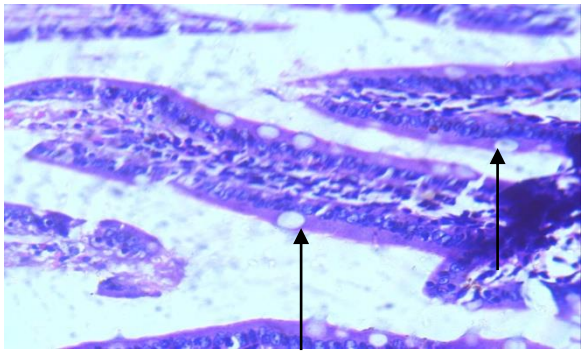

Figure 1: Negative Control of intestine section shows mucosa line by epithelial cell with few goblet cells. H & E X100.

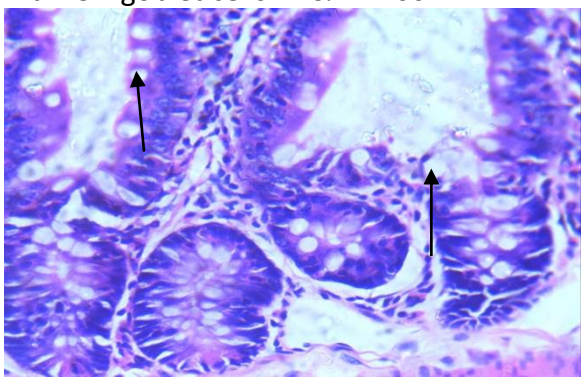

Figure 2: intestine of rats treated with 100mg/kg/28 days, section shows mucosa line by epithelial cell with numerous goblet cells. H & E X100.

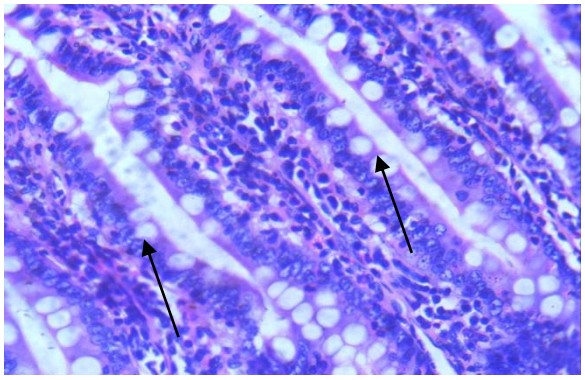

Figure 3: Photomicrograph of rats treated with 200mg/kg/28 days, section shows mucosa line by epithelial cell with numerous goblet cells. H & E X100.

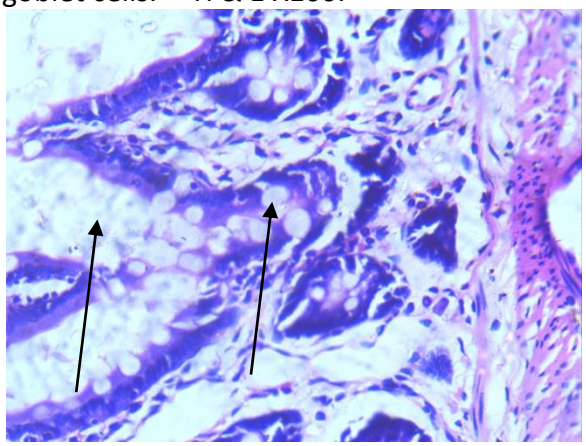

Figure 4: Photomicrograph of rats treated with 300mg/kg/28 days, section shows mucosa line by epithelial cell with numerous goblet cells. H & E X100.

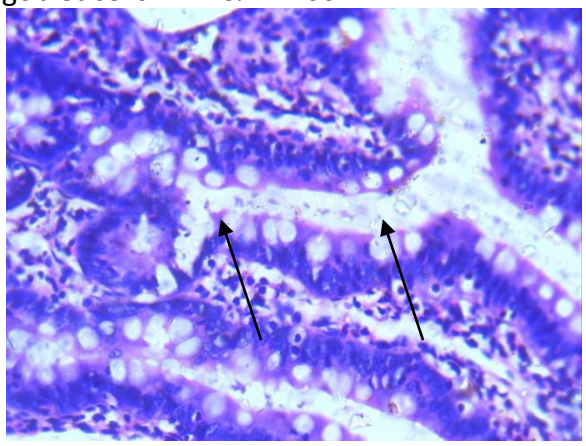

Figure 5: Photomicrograph of rats treated with 400mg/kg/28 days, section shows mucosa line by epithelial cell with numerous goblet cells. H & E X100.

ECRTD-UK https://www.eajournals.org/
ULR: https://doi.org/10.37745/ijcabg.16

DISCUSSION

The present study was aimed at evaluating the effects of aqueous stem bark extract of *Cadabaa farinosa* on the small intestine of adult Wistar rats. In Table 1, the acute toxicity study revealed that oral administration of the extract up to a dose of 5000 mg/ kg produced no immediate signs of toxicity or mortality. The LD_{50} was therefore estimated to be above 5000 mg/kg according to Lorke's [17]. Indicating that aqueous extract of *Cadaba farinosa* could be administered with some degree of safety, especially through oral route where absorption might not be complete due to inherent factors limiting gastrointestinal tract absorption.

In this study, haematological parameters (such as Hgb, RBC, HCT, MCV, MCH, MCHC, WBC, L, and PLT) were investigated in the treated and negative control group. The results revealed no statistically significant differences in haematological parameters between treated and negative control groups. RBC count and RBC indices (Hgb, MCV, MCH and MCHC) observed were not significantly different from negative controls. This result suggests that long term use of aqueous stem bark extract of *Cadaba farinosa* has no differential effect on matured RBCs and change in the rate of production of RBCs (erythropoiesis). The absence of significant difference in the values of RBC and Hgb between treated and negative control group imply that there is no abnormal change in oxygen carrying capacity of RBC and the amount of oxygen delivered to the tissues. This finding was in agreement with reports of Dawit[19] on the effect of sub-chronic administration of methanol extract of *embelia schmperi* in mice; acute and sub-chronic toxicity of e*uphorbia hirta* methanol extract in rats [20] where plant extracts did not alter total RBC count, Hgb, MCV, MCH and MCHC. However, there were slight changes of these parameters among normal animal groups as reported [21].

Histological findings showed normal sections of tissues among study groups. However, considerable goblet cells (mucus secretions) were observed in animals treated with extract compared to negative control. A possible explanation is that Cyclooxygenase pathway 2 (COX2) is activated through PGE2 receptors to produce prostaglandins. The anti-inflammatory action of prostaglandins in the gut ameliorates gastrointestinal mucosal damage [22]. Thus, duodenal and intestinal lesions are prevented which are major risk factor in ulcer disease and gastrointestinal haemorrhage [23]. It is long known that NSAIDs contribute to worsening of gastrointestinal mucosal damage and inflammation in humans and are a major risk factor for ulcer disease and gastrointestinal haemorrhage [24, 25, 26, and 27]. Experimentally, gastric damage are induced by COX inhibitors or ameliorated by PGE2 and EP1 agonists [28, 29]. Duodenal and intestinal lesions are prevented by EP3 and EP4 agonists [30, 31]. Part of the EP4 receptor-mediated intestinal mucosal protection might be due to stimulation of duodenal bicarbonate and mucus secretion [32, 33, and 34]. Its anti-apoptotic effect on epithelial cells [35], vasodilatation [36] and vascular endothelial growth factor (VEGF) release promote angiogenesis and mucosal healing [37].

CONCLUSION

Treatment with aqueous stem bark extract of *Cadaba farinosa* in animal models ameliorates gastrointestinal mucosal damage resulting from reduced mucosal barrier from mucus secretion (anti-peptic ulcer) and further studies to identify the active compound.

References

[1] Ekor Martins, Luisa Pistelli, Zemede Asfaw, Susan Sempele (2014). The Growing Uses of Herbal Medicines: Issues Relating to Adverse Reactions and Challenges in Monitoring Safety. *Frontiers in Pharmacology*. **4**:4-6.

[2] Bandaranayake,W.M., I.Ahmad, F.Aqil., and M. Owais (2006). Quality Control, Screening, Toxicity and Regulation of Herbal Drugs. Turning Medicinal Plants into Drugs. *Modern Phytomedicine.* **2**:25-57.

[3] Vanherweghem J.L and Degaute J.P. (1998). The Policy of Administration to the Education in Medicine and Dentistry in the French Speaking Community of Belgium. *Acta Clin. Belgium.* 53, 2-3.

[3] Vanherweghem J.L and Degaute J.P. (1998). The Policy of Admission to the Education in mMedicine and Dentistry in the French speaking Community of Belgium. *ActaClin.Belg.* 53, 2–3.

[4] Cosyn J.P, Jadoul M, Squifflet J.P, Wese F.X, and Van Perselede C., (19990. Urothelial Lesions in Chinese Herbnephropathy. *American Journal of Kidney Disease*. 33:1011-1017.

[5] Ernst, E (2002). Toxic Heavy Metals and Undeclared Drugs in Asian Herbal Medicines. *Trends Pharmacological Science.* **23**:136-139.

[6] Effendy, W., Siti-Nurtahirah, J., Hussin, Z. (2006). The Side Effects of *Kacip Fatimah* Extract on Liver and Kidney of White Rats. *Journal of Sustainability Science and Management*. **1:**40-46.

[7] Angel Josabad Alonso-Castro, Fabiola Domínguez, Alan Joel Ruiz-Padilla, Nimsi Campos-Xolalpa, Juan Ramón Zapata-Morales, Candy Carranza-Alvarez, and Juan Jose Maldonado-Miranda (2017). Review Article; Medicinal Plants from North and Central America and the Caribbean Considered Toxic for Humans. *Hindawi Evidence Based Complementary and Alternative Medicine.* **2**:1-28.

[8] John, T. A., Okoli, C. C., and Ekor, M. (1997). Some Phytochemical, Safety, Antimicrobial and Haematological Studies of Super B and Seven Keys to Power Blood Purifier Herbal Tonics. *Nigeria Journal of Medical Resources*. 1, 37–43.

[9] Mohammed Z., Daja A, Hamza H, Gidado A., and Hussaini I., (2014). Ethno botanical Survey of Folkloric Plants Used in Managing Breast Cancer by the Traditional Medical Practitioners of North-East Nigeria. *Journal of Medical and Applied Biosciences.* **6**: 29-43.

[10] Viqar Uddin A., Azia ur Rahman A., Shoib A. C., Marie H. M. and Cladry J. (1985), Cadabacine, an alkaloid from *Cadaba farinosa*. *Phytochemistry*. **24**: 2709-2711.

[11] Viqar Uddin A., Kaniz F., Azia ur Rahman A. and Shoib, A. (1987). Cadabacine and cadabacine diacetate from *Crataeva nurvala* and *Cadaba farinosa. Journal of National Production*. **50**:1186.

[12] Ahmad Iqbal, Arina Zafar Beg. (2002). In-vitro fungitoxicity of the essential oil of Syzygium aromaticum. *World Journal of Microbiology and Biotechnology*.**18** (4):317-319.

[13] Nadkarni A.K (2004). Indian Materia Medica. 3rd edition. Bombay. Popular Prakashan. **1**:225-226.

[14] Tenpe CR, Upaganlawar AB, Yeole PG (2006). Antidiabetic activity of *Cadaba indica* in Alloxan induced diabetic rats. *Indian Journal of National Production*. **22**(2):14-17.

[15] Monjane Juliao (2017). Secondary Metabolites from Mozambican Plants: Isolation and Characterization. Printed in Sweden by Media Tryck. Lund University. Centre for Analysis and Synthesis. Pp. 4-25.

[16] Majekodunmi O., Zany K., Olanyaga, I, Shi L and Melanhin J., (1996). Selective Toxicity Diterpene from Euphorbia Poi sonic. *Journal of Medicinal Chemistry.* **39**:1005-1008.

[17] Lorke D., (1983). A New Approach to Practical Acute Toxicity Testing. *Archives of toxicology*. **53**:275-287.

[18] Avwioro O. G., (2014). Histochemistry and Tissue Pathology. Principles and Techniques. 4th Edition. Pp. 123-425.

[19] Dawit, A., Kinfu, Y., Debella, A. (2012). Sub-chronic Toxicity Study of the Crude Methanolic Fruit Extract of *Embelia Schimperi* on Some Blood Parameters, Liver and Kidney of Mice. *LAP LAMBERT Academic Publishing*, Saarbrücken.

[20] Ping,Y., Darah, I., Chen, Y., Sreeramanan, S & Sasidharan, S. (2013). Acute and Subchronic Toxicity Study of *Euphorbia hirta* L. Methanol Extract in Rats. *BioMed Research International*, **182064**:1-14.

[21] Panunto W., Jaijoy K., Lerdvuthisopon N., Lertprasertsuke N., Jiruntanat N, Soonthornchareonnon N., Sireeratawong S. (2011). Acute and Chronic Toxicity Studies of the Water Extract from Dried Fruits of *Terminalia chebula Rezt* in rats. *International Journal of Applied Research in Natural Products*. **3**:36-43.

[22] Morteau, O., Morham, S. G., Sellon, R., Dieleman, L. A., Langenbach, R., Smithies, O., (2000). Impaired Mucosal Defence to Acute Colonic Injury in Mice Lacking Cyclooxygenase-1 or Cyclooxygenase-2. *Journal of Clinical Investigations*. 105:469–478.

[23] Viktoria Konya, Gunther Marsche, Rufina Schuligoi, Akos Heinemann (2013). E-type prostanoid receptor 4 (EP4) in disease and therapy. *Journal of Pharmacology & Therapeutics* **138** (2013):485–502.

[24] Kaufmann, H. J., & Taubin, H. L. (1987). Nonsteroidal anti-inflammatory drugs activate quiescent inflammatory bowel disease. Ann Intern Med 107, 513–516.

[25] Bjarnason, I., Hayllar, J., Macpherson, A. J., & Russell, A. S. (1993). Side-effects of nonsteroidal anti-inflammatory drugs on the small and large-intestine in humans. Gastroenterology 104, 1832–1847.

[26] Felder, J. B., Korelitz, B. I., Rajapakse, R., Schwarz, S., Horatagis, A. P., & Gleim, G. (2000). Effects of Nonsteroidal Antiinflammatory Drugs on Inflammatory Bowel Disease: A Case–Control Study. *American Journal of Gastroenterololgy*. 95, 1949–1954.

[27] Laine, L., Takeuchi, K., & Tarnawski, A. (2008). Gastric mucosal defense and cytoprotection: bench to bedside. Gastroenterology 135, 41–60.

[28] Suzuki, K., Araki, H., Mizoguchi, H., Furukawa, O., & Takeuchi, K. (2001). Prostaglandin E inhibits indomethacin-induced gastric lesions through EP-1 receptors. Digestion 63, 92–101.

[29] Takeuchi, K., Araki, H., Umeda, M., Komoike, Y., & Suzuki, K. (2001). Adaptive gastric cytoprotection is mediated by prostaglandin EP1 receptors: a study using rats and knockout mice. J Pharmacol Exp Ther 297, 1160–1165.

[30] Kunikata, T., Araki, H., Takeeda, M., Kato, S., & Takeuchi, K. (2001). Prostaglandin E prevents indomethacin-induced gastric and intestinal damage through different EP receptor subtypes. J Physiol Paris 95, 157–163.

[31] Kunikata, T., Tanaka, A., Miyazawa, T., Kato, S., & Takeuchi, K. (2002). 16,16-Dimethyl prostaglandin E2 inhibits indomethacin-induced small intestinal lesions through EP3 and EP4 receptors. Dig Dis Sci 47, 894–904.

[32] Takeuchi, K., Yagi, K., Kato, S., & Ukawa, H. (1997). Roles of prostaglandin E-receptor subtypes in gastric and duodenal bicarbonate secretion in rats. Gastroenterology 113, 1553–1559.

[33] Araki, H., Ukawa, H., Sugawa, Y., Yagi, K., Suzuki, K., & Takeuchi, K. (2000). The roles of prostaglandin E receptor subtypes in the cytoprotective action of prostaglandin E2 in rat stomach. Aliment Pharmacol Ther 14(Suppl. 1), 116–124.

[34] Aihara, E., Nomura, Y., Sasaki, Y., Ise, F., Kita, K., & Takeuchi, K. (2007). Involvement of prostaglandin E receptor EP3 subtype in duodenal bicarbonate secretion in rats. Life Sci 80, 2446–2453.

[35] Hoshino, T., Tsutsumi, S., Tomisato, W., Hwang, H. J., Tsuchiya, T., & Mizushima, T. (2003). Prostaglandin E2 protects gastric mucosal cells from apoptosis via EP2 and EP4 receptor activation. J Biol Chem 278, 12752–12758.

[36] Hattori, Y., Ohno, T., Ae, T., Saeki, T., Arai, K., Mizuguchi, S., et al. (2008). Gastric mucosal protection against ethanol by EP2 and EP4 signaling through the inhibition of leukotriene C4 production. Am J Physiol Gastrointest Liver Physiol 294, G80–G87.

[37] Hatazawa, R., Tanaka, A., Tanigami, M., Amagase, K., Kato, S., Ashida, Y., et al. (2007). Cyclooxygenase-2/prostaglandin E2 accelerates the healing of gastric ulcers via EP4 receptors. Am J Physiol Gastrointest Liver Physiol 293, G788–G797.