

Documents

Aksoy, N.^a, Sen, E.^b, Sukmasari, S.^c, Özakpınar, Ö.B.^d, Arıcıoğlu, F.^e, Yücel, Y.Y.^b, Dumlu, M.R.^f, Doolaanea, A.A.^g, AbdulRahman, M.N.^h, Olgac, V.ⁱ, Bozkan, P.^j, Ozen, B.^j^k

Investigation of the protective effect of gel incorporating *Eugenia jambolana* leaf extract on 5-fluorouracil-induced oral mucositis: an animal study

(2022) *Journal of Cancer Research and Clinical Oncology*, 148 (8), pp. 2153-2162.

DOI: 10.1007/s00432-022-04065-3

^a School of Pharmacy, Department of Clinical Pharmacy, Altınbaş University, Zuhuratbaba, Incirli Cd. No:11-A, Istanbul, 34147, Turkey

^b School of Pharmacy, Department of Biochemistry, Altınbaş University, Istanbul, Turkey

^c Pediatric Dentistry Department and Dental Public Health Department, International Islamic University Malaysia, Kuantan, Malaysia

^d School of Pharmacy, Department of Biochemistry, Marmara University, Istanbul, Turkey

^e Institute of Health Sciences, Marmara University, Istanbul, Turkey

^f Department of Infectious Disease and Clinical Microbiology, University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Istanbul, Turkey

^g Department of Pharmaceutical Technology, Faculty of Pharmacy, International Islamic University, Kuantan, Malaysia

^h Faculty of Pharmacy, PICOMS International University College, Kuala Lumpur, Malaysia

ⁱ Institute of Oncology, Department of Tumor Pathology, Istanbul University, Istanbul, Turkey

^j Department of Pediatric Dentistry, Faculty of Dentistry, Altınbaş University, Istanbul, Turkey

^k Department of Pediatric Dentistry, Faculty of Dentistry, Istanbul Health and Technology University, Istanbul, Turkey

Abstract

Purpose: The study aimed to evaluate the possible preventive effect of two concentrations (3 and 5% w/w) of *Eugenia jambolana* (EJ) extract against 5-FU-induced mucositis. Method: Sixteen adult rats were separated into four groups: two control and two preventive groups. Animals in Groups 1, 2, and 3 were injected intraperitoneally with 60 mg/kg/day of 5-FU on Day 1 followed by 150 mg/kg/day on Day 5. The rats in Group 4 (negative control) were given physiological saline at the same times and doses. Furthermore, on the fifth day of the study, the cheek and sublingual mucosa were irritated by external superficial scratches using the tip of an 18-G needle, followed by the application 15 µL of 20% acetic acid, after which 3 and 5% EJ w/w gels were applied topically for animals in Groups 2 and 3, respectively. Results: The weight and the mucositis scores were recorded. Antioxidant and anti-inflammatory markers and biochemical tests were analyzed. Significant differences were found between the study groups in weight loss, clinical mucositis scores, mortality rates, and antioxidant and anti-inflammatory parameters. Conclusion: The preventive effect of 3% gel was significant, with no mortality rate, making it an option for preventive strategies. © 2022, The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature.

Author Keywords

Anti-inflammatory; Antioxidant; Chemotherapy; *Eugenia jambolana*; Gel; Mucositis

Index Keywords

antiinflammatory agent, antioxidant, fluorouracil, plant extract; adverse event, animal, gel, mucosa inflammation, rat, stomatitis, *Syzygium*; Animals, Anti-Inflammatory Agents, Antioxidants, Fluorouracil, Gels, Mucositis, Plant Extracts, Rats, Stomatitis, *Syzygium*

Chemicals/CAS

fluorouracil, 51-21-8; Anti-Inflammatory Agents; Antioxidants; Fluorouracil; Gels; Plant Extracts

References

- Anand, H., Misro, M.M., Sharma, S.B., Prakash, S.
Cytoprotective effects of fruit pulp of *Eugenia jambolana* on H₂O₂-induced oxidative stress and apoptosis in rat leydig cells in vitro
(2012) *Andrologia*, 45 (3), pp. 145-157.
- Anatoliotakis, N., Deftereos, S., Bouras, G., Giannopoulos, G., Tsounis, D., Angelidis, C., Kaoukis, A., Stefanadis, C.
Myeloperoxidase: expressing inflammation and oxidative stress in cardiovascular

disease

(2013) *Curr Top Med Chem*, 13 (2), pp. 115-138.

- Asadullah, K., Sterry, W., Volk, H.D.
Interleukin-10 therapy—review of a new approach
(2003) *Pharmacol Rev*, 55 (2), pp. 241-269.
- Baliga, M.S., Bhat, H.P., Baliga, B.R.V., Wilson, R., Palatty, P.L.
Phytochemistry, traditional uses and pharmacology of *Eugenia jambolana lam.* (Black Plum): a review
(2011) *Food Res Int*, 44 (7), pp. 1776-1789.
- Beutler, E.
Improved method for the determination of blood glutathione
(1963) *J Lab Clin Med*, 61, pp. 882-888.
COI: 1:CAS:528:DyaF3sXksV2rsbo%3D, PID: 13967893
- Cheng, K.K.F.
Oral mucositis, dysfunction, and distress in patients undergoing cancer therapy
(2007) *J Clin Nurs*, 16 (11), pp. 2114-2121.
- Collins, F.S., Varmus, H.
A new initiative on precision medicine
(2015) *N Engl J Med*, 372 (9), pp. 793-795.
COI: 1:CAS:528:DC%2BC2MXjvFGnsLY%3D
- Da Cruz Campos, M., Campos, C., Corrêa, J.O., Aarestrup, F., Aarestrup, B.
Induced oral mucositis in wistar rats treated with different drugs: preventive potential in cytokine production
(2021) *Mol Clin Oncol*, 14 (6), p. 127.
- Dos Reis, P.E.D., Ciol, M.A., De Melo, N.S., Figueiredo, P.T.D.S., Leite, A.F., Manzi, N.D.M.
Chamomile infusion cryotherapy to prevent oral mucositis induced by chemotherapy: a pilot study
(2016) *Support Care Cancer*, 24 (10), pp. 4393-4398.
- Ito, F., Sono, Y., Ito, T.
Measurement and clinical significance of lipid peroxidation as a biomarker of oxidative stress: oxidative stress in diabetes
(2019) *Atheroscler Chronic Inflamm Antioxid*, 8 (3), p. 72.
- Jay, D., Hitomi, H., Griendling, K.K.
Oxidative stress and diabetic cardiovascular complications
(2006) *Free Rad Biol Med*, 40 (2), pp. 183-192.
- Keefe, D.M.K., Brealey, J., Goland, G.J., Cummins, A.
Chemotherapy for cancer causes apoptosis that precedes hypoplasia in crypts of the small intestine in humans
(2000) *Gut*, 47 (5), pp. 632-637.
COI: 1:CAS:528:DC%2BD3cXosVSgtbk%3D
- Logan, R.M., Gibson, R.J., Sonis, S.T., Keefe, D.M.K.
Nuclear factor-kappaB (Nf-KappaB) and cyclooxygenase-2 (Cox-2) expression in the oral mucosa following cancer chemotherapy
(2007) *Oral Oncol*, 43 (4), pp. 395-401.
- Logan, R.M., Stringer, A.M., Bowen, J.M., Gibson, R.J., Sonis, S.T., Keefe, D.M.K.
Serum levels of Nf-Kb and pro-inflammatory cytokines following administration of mucotoxic drugs
(2008) *Cancer Biol Ther*, 7 (7), pp. 1139-1145.

- Moore, K.W., De Waal Malefyt, R., Coffman, R.L., O'garra, A.
Interleukin-10 and the interleukin-10 receptor
(2001) *Annu Rev Immunol*, 19 (1), pp. 683-765.
- Münstedt, K., Momm, F., Hübner, J.
Honey in the management of side effects of radiotherapy-or radio/chemotherapy-induced oral mucositis. A systematic review
(2019) *Complement Ther Clin Pract*, 34, pp. 145-152.
- Nandi, A., Yan, L.-J., Jana, C.K., Das, N.
Role of catalase in oxidative stress- and age-associated degenerative diseases
(2019) *Oxid Med Cell Longev*, 11, pp. 1-19.
- O'reilly, M., Mellotte, G., Ryan, B., O'connor, A.
Gastrointestinal side effects of cancer treatments
(2020) *Ther Adv Chronic Dis*, 11.
2040622320970354
- Parkins, C.S., Fowler, J.F., Yu, S.
A murine model of lip epidermal/mucosal reactions to X-irradiation
(1983) *Radiother Oncol*, 1 (2), pp. 159-165.
- Pulito, C., Cristaudo, A., Porta, C.L., Zapperi, S., Blandino, G., Morrone, A., Strano, S.
Oral mucositis: the hidden side of cancer therapy
(2020) *J Exp Clin Cancer Res*, 39 (1), p. 210.
- Rahman, F., Baishnab, S.
Comparative study of Eugenia Jambolana seed and pulp for antidiabetic action on alloxan induced diabetic rats
(2016) *Int J Basic Clin Pharmacol*,
- Rani, V., Gupta, A., Awasthi, S., Suneja, T., Yadav, M., Verma, S.
Antidiabetic activity of indian medicinal plants
(2020) *Herbal Medicine In India*, pp. 155-174.
Springer, Singapore
- Raval, J.K., Prasad, M., Parmar, H.C., Patel, J.M., Vihol, P.D., Patel, J.H., Kalyani, I.
Ameliorative effects of Eugenia Jambolana seeds aqueous extract on diabetes induced oxidative stress in rats
(2019) *Haryana Vet*, 58 (2), pp. 232-235.
- Richard, M.J., Portal, B., Meo, J., Coudray, C., Hadjian, A., Favier, A.
Malondialdehyde Kit evaluated for determining plasma and lipoprotein fractions that react with thiobarbituric acid
(1992) *Clin Chem*, 38 (5), pp. 704-709.
DOI: 10.1093/clin/38.5.704
- Sahebamee, M., Mansourian, A., Hajimirzamohammad, M., Zadeh, M.T., Bekhradi, R., Kazemian, A., Doroudgar, K.
Comparative efficacy of aloe vera and benzydamine mouthwashes on radiation-induced oral mucositis: a triple-blind, randomised, controlled clinical trial
(2015) *Oral Health Prev Dent*, 13 (4), pp. 309-315.
PID: 25431805
- Sankhari, J.M., Jadeja, R.N., Thounaojam, M.C., Devkar, R.V., Ramachandran, A.V.
Eugenia Jambolana seed extract supplementation attenuates cardiac and hepatic oxidative stress and pathophysiological changes in hypercholesterolemic rats
(2012) *Orien Pharm Exp Med*, 12 (2), pp. 99-106.
- Sharma, B., Viswanath, G., Salunke, R., Roy, P.

Effects of flavonoid-rich extract from seeds of *Eugenia Jambolana* (L.) on carbohydrate and lipid metabolism in diabetic mice

(2008) *Food Chemistry*, 110 (3), pp. 697-705.

- Sharma, P., Jhawar, V., Mathur, P., Dutt, R.
Innovation in cancer therapeutics and regulatory perspectives
(2022) *Med Oncol*, 39 (5), pp. 1-12.
- Sharma, R.J., Gupta, R.C., Singh, S., Bansal, A.K., Singh, I.P.
Stability of anthocyanins-and anthocyanidins-enriched extracts, and formulations of fruit pulp Of *Eugenia Jambolana* ('Jamun')
(2016) *Food Chem*, 190, pp. 808-817.
COI: 1:CAS:528:DC%2BC2MXhtVSqu7jP
- Silverman, S.
Diagnosis and management of oral mucositis
(2007) *J Support Oncol*, 5, pp. 13-21.
COI: 1:CAS:528:DC%2BD2sXivF2rtro%3D, PID: 17366929
- Siomek, A., Tujakowski, J., Gackowski, D., Rozalski, R., Foksinski, M., Dziaman, T., Roszkowski, K., Olinski, R.
Severe oxidatively damaged Dna after cisplatin treatment of cancer patients: cisplatin-induced dna damage
(2006) *Int J Cancer*, 119 (9), pp. 2228-2230.
- Sonis, S.T.
A biological approach to mucositis
(2004) *J Support Oncol*, 2 (1), pp. 21-32.
PID: 15330370
- Sonis, S.T.
Oral mucositis in cancer therapy
(2004) *J Support Oncol*, 2, pp. 3-8.
PID: 15605918
- Sonis, S.T.
Pathobiology of oral mucositis: novel insights and opportunities
(2007) *J Support Oncol*, 5, pp. 3-11.
COI: 1:CAS:528:DC%2BD2sXhtlOhsb3K, PID: 18046993
- Stephens, J.W., Khanolkar, M.P., Bain, S.C.
The biological relevance and measurement of plasma markers of oxidative stress in diabetes and cardiovascular disease
(2009) *Atherosclerosis*, 202 (2), pp. 321-329.
- Sukmasari, S., Mohd, F.N., Qader, O.A.J.A., Rahman, M.N.A.
Total phenolic content, flavonoid content, and antioxidant capacity of *Syzygium cumini* (L.) skeels leaves grown in Wonosobo, java, Indonesia and comparison against current findings of *Syzygium cumini* leaves and *Syzygium polyanthum* (Wight) walp Leaves
(2018) *Journal Of Pharmaceutical Sciences And Research*, 10 (1), pp. 31-35.
COI: 1:CAS:528:DC%2BC1cXitFKrt7rP
- Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A., Bray, F.
Global cancer statistics 2020: globocan estimates of incidence and mortality worldwide for 36 cancers in 185 Countries
(2021) *A Cancer J Clin*, 71 (3), pp. 209-249.
- (2019) *Turkstat, Turkish Statistical Institute, Cause of Death Statistics*, Accessed 05 May 2022

- Vanlancker, E., Vanhoecke, B., Smet, R., Props, R., Van De Wiele, T.
5-Fluorouracil sensitivity varies among oral micro-organisms
(2016) *J Med Microbiol*, 65 (8), pp. 775-783.
DOI: 10.1093/jmm/65.8.775

- Villa, A., Sonis, S.T.
Pharmacotherapy for the management of cancer regimen-related oral mucositis
(2016) *Expert Opin Pharmacother*, 17 (13), pp. 1801-1807.

Correspondence Address

Aksoy N.; School of Pharmacy, Zuhuratbaba, Incirli Cd. No:11-A, Turkey; email: nilay.aksoy@altinbas.edu.tr

Publisher: Springer Science and Business Media Deutschland GmbH

ISSN: 01715216

CODEN: JCROD

PubMed ID: 35622166

Language of Original Document: English

Abbreviated Source Title: J. Cancer Res. Clin. Oncol.

2-s2.0-85130847543

Document Type: Article

Publication Stage: Final

Source: Scopus

ELSEVIER

Copyright © 2022 Elsevier B.V. All rights reserved. Scopus® is a registered trademark of Elsevier B.V.

 RELX Group™