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Anti-inflammatory effect of ethanolic extract of *Ocimum basilicum* L. in the healing process of incisional wounds in mice

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Maintaining the structural and functional integrity of the skin is critical to ensure body homeostasis. After damage, a series of cellular and molecular events occurs in this structure in order to repair the injured tissue. Imbalances in one or more repair steps are commonly related to difficulties in proceeding with healing. This has driven the search for natural molecules from plants to improve the repair process that is economical with less side effects. In this context, the common medicinal herb, *Ocimum basilicum* L., used globally from cooking to practices in folk medicine, has in its phytoconstitution substances with different actions such as anti-inflammatory, antioxidant, antimicrobial. Therefore, in the present study, we have evaluated the anti-inflammatory effect of intraperitoneal treatment with ethanolic extract of *O. basilicum* (EEOB) on wound healing in mice. Incisional wounds were induced in mice, they were divided according to treatment period and group, n=6, and received EEOB intraperitoneally (i.p.) at 150 mg/kg daily or saline solution for 5 or 7 days. At the end of this period, the animals were euthanized and the lesions underwent histopathological processing and analysis. In animals treated with EEOB injection, there was a decrease in the number of leukocytes at 5 days and mast cells at 7 days post-injury compared to the control. The observed anti-inflammatory action can be attributed to the phenolic compounds and their individual or synergistic effects on the healing process.

Keywords: Basil, Inflammation, Wound healing

The skin is an organ that has important and essential characteristics for the physiology of the human body, in addition to being considered one of the largest organs[1], therefore, maintaining its integrity is essential for the maintenance of the organism's homeostasis. Its structure features a series of cells and molecules capable of preventing damage. Keratinocytes, melanocytes, sebaceous glands and defense cells are able to provide protection to such a structure in several ways, either by hypermeabilizing, protecting from solar radiation or entry of pathogens[2,3].

This external barrier to the body is subject to suffering various traumas that can disrupt its organization and in function. In view of this, the healing of cutaneous wounds is the result of a set of cellular and molecular events, which, together, aim at the reconstruction of the injured tissue, replacing it with a new vascularized connective tissue[4]. In this process, the phases are identified: inflammatory, proliferative and remodeling.

In the inflammatory stage, hemostasis and leukocyte migration occur, in which neutrophils reach the lesion site and, later, macrophages, which phagocytize cell debris, eliminate pathogens and recruit fibroblasts to the site and, if there is a compromise between the transition from this to the next stage, the chances of unwanted changes in the final result of this process or the possibility of not even achieving it are relatively high[5]. In the proliferative phase, migration and proliferation of fibroblasts, deposition of granulation tissue, angiogenesis and re-epithelialization occur. At this stage, growth factors such as VEGF, TGF-β1, and FGF are essential for cell signaling and activity[6,7]. The last step, which can take from months to years, is remodeling, the final phase of the healing process, which results in a remodeled scar in which type III collagen is replaced by type I collagen, providing greater resistance to the injured area[8,9]. The consequences of changes on the healing process have

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long been discussed, for example, prolonged inflammation can trigger problems such as the formation of keloids and hypertrophic scars or even a delay in the repair process[10]. Thus, the search for treatments that aim to accelerate or improve this process has been constant. In this sense, the use of plant extracts as a therapy, considering the individual or collective effects of tissue repair, in parallel with the possibility of reducing side effects, is promising in the treatment of wounds[11,12].

Ocimum basilicum, known in some regions as basil, belongs to the Lamiaceae family and has a wide distribution, being found in Tropical Asia, Africa, Central America and South America. Commercially, the species is offered as a flavoring or condiment prepared from green and aromatic leaves, which can be used fresh or dried[13,14]. In the literature, studies describe *O. basilicum* for its anti-inflammatory, antifungal, antioxidant and antibacterial properties[15,16]. The anti-inflammatory activity has been demonstrated in several experimental models, *in vivo* and *in vitro*, with the main effect of reducing the infiltration of inflammatory cells, reducing edema and the release of chemical mediators, such as nitric oxide[14,17-]. These properties are related to the presence of phenolic compounds[22,23], tannins and flavonoids[23-25]. Therefore, in this study, we evaluated the anti-inflammatory effect the ethanolic extract of *Ocimum basilicum* on wound healing in mice.

Materials and Methods

Preparation of the ethanolic extract

For preparation of the extract, aerial parts of the species *Ocimum basilicum* L. were collected in the city of Carmópolis de Minas, Minas Gerais, Brazil, identified by Prof. Alexandre Salino, and an exsiccate was deposited in the Herbarium of Instituto de Ciências Biológicas da Universidade Federal de Minas Gerais, with the registration number BHCB 147240. This study has permission to access the components of the plant genetic heritage and is registered on the PlatformSisGen (A715CDC), (13.123/2015), according to Brazilian Biodiversity Law (13.123/2015).

A total of 110.85 g of fresh plant material was ground and left to macerate for 10 days in P.A. ethanol. After this period, the material was filtered and dried in rotary steamer obtaining 5.56 g of ethanol extract. The extract was qualitatively screened for the presence of different classes of natural products such as alkaloids, steroids, triterpenoids, coumarins, tannins, saponins and flavonoids[26]. The total phenolic content of ethanolic extract was determined using the Folin-Dennis reagent with tannic acid as the standard and result was expressed as tannic acid equivalents/mL[27]. The volatile compounds from ethanolic extract were analyzed by gas chromatography/mass spectrometry (GC/MS), and identified by mass spectral database search (NIST) followed by matching of MS data and expressed in relative percentage of each compound, calculated by internal normalization of the chromatographic peak area[28]. Solutions for the treatment of animals were obtained by resuspension of this extract in saline solution (NaCl 0.9%).

Animals

All experiments were performed in accordance with the Guide for the Care and Use of Laboratory Animals and were approved by the Animal Ethics Committee of the Federal University of São João del-Rei (UFSJ, Brazil, protocol 008/2017). Thirty-six male mice (Swiss strain), weighing 30 to 40 g, were obtained from the Center for Bioterism at the Dom Bosco *Campus* of UFSJ and kept under standard temperature conditions (20 to 24°C) and light/dark cycle, with solid feed and water ad libitum. The animals were randomly divided into two groups of 12 animals each: Control Group and Experimental Group. Each group was subdivided into two other subgroups according to the euthanasia period: 5/7 days.

Incisional wound

Initially, the mice were anesthetized with an intraperitoneal (i.p.) injection of ketamine (97 mg/kg) and xylazine (16.5 mg/kg), then placed on a surgical board in the prone position for the surgical procedure. Trichotomy of the dorsal and thoracic hairs was performed. The skin was cleaned with 70% ethanol and then a linear incision was made with a 1.0 cm scalpel blade on the paramedial surface of the back of each mouse. Hemostasis was performed by pressing sterile gauze over the operative wound, which was left with a dressing (Micropore 3M).

Treatment with ethanolic extract of *Ocimum basilicum*

Immediately after the production of lesions, the animals began to receive the treatment assigned to each group. The animals in the experimental group received a daily intraperitoneal injection of the ethanolic extract of *O. basilicum* (EEOB), at a concentration of 150 mg/kg of body wt., and the control group received saline (vehicle) also

intraperitoneally. After 5 and 7 days, 6 animals from each group (Control and Experimental) were randomly selected and euthanized by a lethal dose of anesthetic.

Histopathological analysis

After euthanasia, the fragments containing the surgical wound in all its length and depth were removed with the aid of a number 11 scalpel blade and fixed in a 10% buffered formalin solution for 24 h, sectioned perpendicularly in its half and the pieces separated were dehydrated in successive ethanol solutions and embedded in paraffin. The paraffin blocks were sectioned using a microtome, obtaining 5 µm sections, which were later stained with Hematoxylin & Eosin (H&E) and Toluidine Blue to evaluate the histopathological aspects. Slides were obtained from each wound and evaluated for healing area, re-epithelialization, presence of inflammatory infiltrate, fibroblasts and mast cells in the two observation periods (5 and 7 days). Quantitative analysis of leukocytes, fibroblasts, and mast cells (all identified from their characteristic morphology) was performed using Image J Image Analysis Software (version 1.44, Research Services Branch, U.S. National Institutes of Health, Bethesda, MD, USA.). The images were generated by a light microscope (Motic) connected to a digital camera (Moticam 580 5.0 MP) connected to an on-board computer scanner. A total of five fields per case/slide were analyzed at 400X magnification, within the wound healing area. Results are expressed per group as number of cells/μm^2.

Statistical analysis

For statistical analysis, the Graph Pad Prism 5 Software (GraphPad Software, CA, USA) was used, in which the unpaired 't' test was performed to analyze the differences between the two groups (Physiological solution i.p. and EEOB i.p.). The data obtained are expressed as mean ± standard deviation, considering significant values when $P < 0.05$.

Results and Discussion

The phytochemical screening of the ethanolic extract from basil showed the presence of steroids, triterpenes, flavonoids, alkaloids and coumarins[26] and a total phenolic compounds content of 84.9 µg equivalent of tannic acid/mL of extract[27]. In this extract was identified volatile compounds by GC-MS, such as phytol (44.18%), ethyl linolenate (26.10%), cadinene (11.08%), methyl 2,4,6,8-tetramethyldecanoate (4.66%), methyl 4-ethenyl-benzoate (4.1%), *trans*-methyl cinnamate (2.5%), and 5-methyl-4-hexen-3-one (1.6%)[28].

The present study was carried out to evaluate the anti-inflammatory effect of the ethanolic extract of *O. basilicum* on the healing of experimentally induced wounds in mice. Initially, a qualitative assessment of the repair process was performed, followed by a quantitative analysis of the cells that participate in the recovery of tissue architecture.

Figure 1 illustrates the histopathological analyses of the HE-stained skin sections. On the 5th day after making the lesion, the treated group showed a reduction in the inflammatory infiltrate, while the control group, which did not receive the extract, presented foci of exudation and extensive areas of inflammatory infiltrate, where we clearly observed the presence of the lesion. On the 7th day after making the lesion, the treated group presented re-epithelialization and better deposition of collagen fibres in the granulation tissue, demonstrating a more advanced repair process than the control group, which presented extensive areas of inflammatory infiltrate and did not present complete epithelization. Similarly, a study[29] testing the effects of intradermal injections of oleuropein on the healing of incisional cutaneous wounds in elderly male balb/c mice demonstrated that

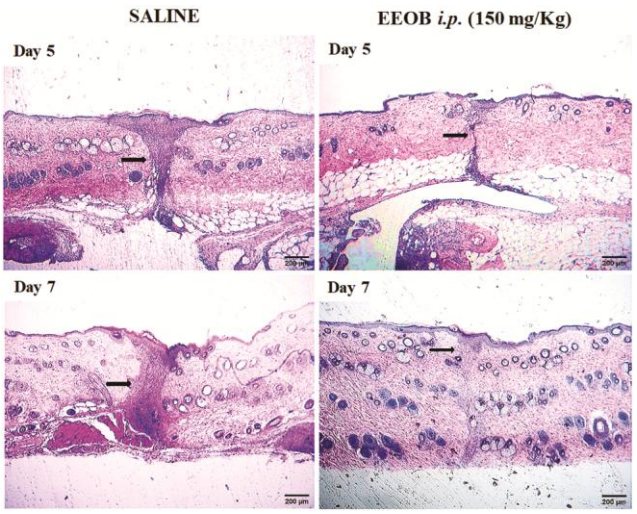

Fig. 1 — Anti-inflammatory effect of ethanolic extract of *Ocimum basilicum* L. (basil) (EEOB) aerial parts at the healing process of incisional wounds in mice. Photomicrographs wounds at day 5 and day 7 after skin injury in mice. Control group, received daily saline solution. EEOB group, received daily basil extract at 150 mg/kg intraperitoneally. The arrows indicate inflammatory infiltrate in the area of the lesion. Haematoxylin & eosin staining, 40X magnification, scale bars: 200 µm.

oleuropein, in addition to reducing inflammation after 3 and 7 days of treatment and increasing VEGF (factor of vascular endothelium growth), in Van Gieson-stained sections after incision, it was observed that oleuropein had a positive effect on type 1 collagen fibre synthesis.

Figure 2 demonstrates the quantitative analyzes of total leukocytes (mono and polymorphonuclear) and fibroblasts. On day 5, the inflammatory infiltrate in the region of the incisional lesion was significantly lower in the EEOB-treated group (2.45±0.35) compared to the control group (4.44±0.55). On day 7, no statistically significant differences were observed between groups (Control: 2.62±0.24 *vs.* EEOB: 2.69±0.72). In the quantification of the fibroblasts analyzed, there were significant differences between the groups, with a mean of 2.77±0.75 in the control group at 5 days, and 1.94±0.32 in the EEOB group; and at 7 days, the mean was 2.34±0.78 in the control group and 1.49±0.24 in the EEOB-treated group.

Similarly, the studies with the effects of an ointment based on an aqueous extract of *O. basilicum* in Sprague-Dawley rats with lesions for 10, 20 and 30 days after surgery, observed a positive action of the plant throughout the healing process, as a lower infiltrate, inflammation and reduction of the lesion area[19]. The measured NO production in RAW 264.7 macrophages, where they detected a reduction in NO in those media that were under the effects of the ethanolic extract of calluses and leaves of *O. basilicum*, confirming anti-inflammatory action on such cells[18]. In this sense, it can be said that the species may have a local action on the inflammatory step in the repair process.

Mast cells are cells that participate in the repair process, including in fetal wounds. Studies in fetuses with lesions and deficient for these cells, present a scar reduction at 7 and 10 days[30]. Figure 3 illustrates

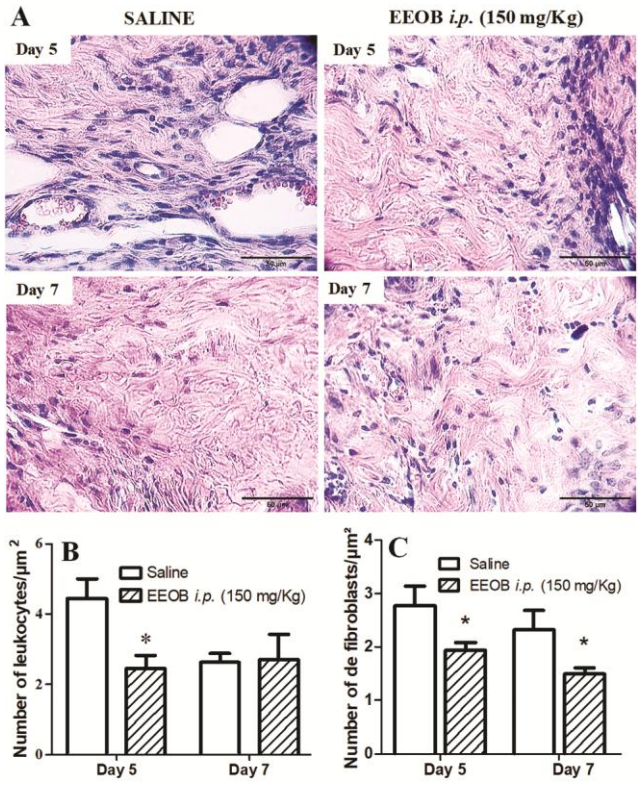

Fig. 2 — Ethanolic extract of *Ocimum basilicum* L. (basil) (EEOB) aerial parts reduced the number of leukocytes and fibroblasts at the healing process of incisional wounds in mice. (A) Photomicrographs wounds at day 5 and day 7 after skin injury in mice. Control group, received daily saline solution. EEOB group, received daily basil extract at 150 mg/kg intraperitoneally. Haematoxylin & eosin staining, 400X magnification, scale bars: 50 µm. (B) Morphometric analysis of number the leukocytes/µm². (C) Morphometric analysis of number the fibroblasts/µm². n=6; **P* ≤0,05 compared with saline group.

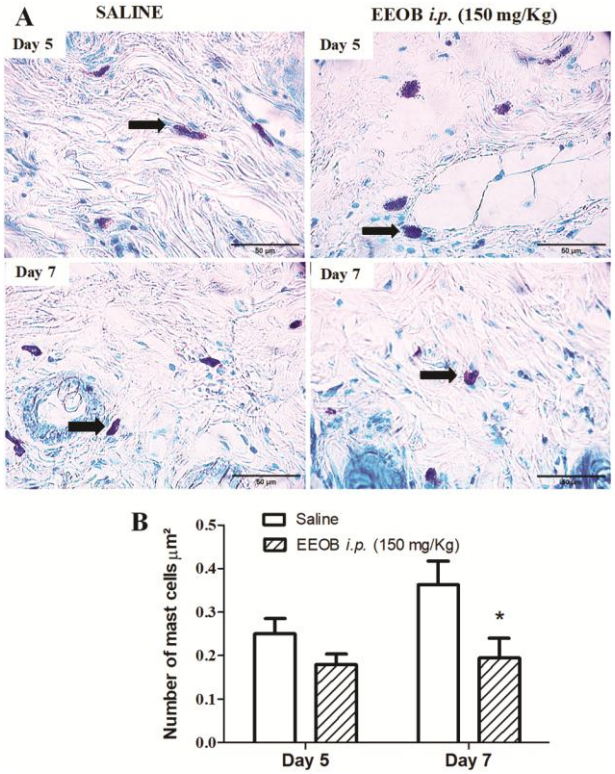

Fig. 3 — Ethanolic extract of *Ocimum basilicum* L. (basil) (EEOB) aerial parts reduces the number of mast cells after 7 days of treatment in incisional wounds in mice. (A) Photomicrographs wounds at day 5 and day 7 after skin injury in mice. Control group, received daily saline solution. EEOB group, received daily basil extract at 150 mg/kg intraperitoneally. The arrows indicate mast cells in the area of the lesion. Toluidin blue staining, 400X magnification, scale bars: 50 µm. (B) Morphometric analysis of number the mast cells/µm². n=6; **P* ≤0,05 compared with saline group.

the histopathological analyzes of the skin sections stained with Toluidine Blue. Mast cells were found in greater numbers in the areas most marginal to the repair zone, while few of these cells were found close to the lesion, being identified from their dark blue staining. Quantitative analyzes of the number of mast cells indicated that there was no statistically significant difference (p=0.1283) between the control (0.2502±0.03487) and i.p. with EEOB (0.1792±0.02485), on the 5th day after the injury. However, at day 7, the mean mast cell population in the region was significantly lower (p=0.0407) in the i.p. with EEOB (0.1938±0.04630), in relation to the control group (0.3627±0.05498). Mast cells can act on injured tissue by secreting factors such as TGF-β[31], participating in the recruitment of fibroblasts[32] and keratinocytes[33] and inducing inflammatory responses[34].

In our study, the daily administration of the ethanolic extract of *O. basilicum* @150 mg/kg of body wt., demonstrated a reduction in the inflammatory process in the initial days of wound healing in mice, represented by the reduction in the number of leukocytes at five days and a reduction in mast cells at 7 days. Some studies have suggested that immune modulation and inflammation reduction act positively during the healing process by reducing the number of granulocytes, mast cells, and improving matrix deposition and scar-free repair[35,36].

The complex of *O. basilicum* essential oil with β-cyclodextrins, at a dose of 10 mg/kg, significantly inhibits the recruitment of lymphocytes, monocytes and granulocytes in a model of carrageenan-induced peritonitis in mice[37]. Similarly, reported that treatment with 3% *O. basilicum* aqueous extract ointment reduced neutrophil and lymphocyte levels during skin wound healing in rats[19].

This reduction in the number of leukocytes and mast cells was probably due to the synergistic action of the phytochemicals present in basil[38-40]. These detected compounds may be responsible for the anti-inflammatory activity. Phenolic compounds, such as phenolic acids and flavonoids exhibit anti-inflammatory activity[41]. Flavonoids present in the species have anti-inflammatory activity, as they inhibit the synthesis of inflammatory mediators and enzymes, such as prostaglandins, protein C and adhesion molecules[42,43]. Other phenolic compounds, such as tannins, also have anti-inflammatory and healing potential. The *Ocimum basilicum* tannins added to a cream showed good effects on wound healing, burn and incisional injury in rabbits, due to increased fibroblast infiltration and good collagen deposition, in addition, these compounds induce a reduction in the synthesis of mediators inflammatory[44,45].

Conclusion

Results of the present study have demonstrated that administration of ethanolic extract of *Ocimum basilicum* @150 mg/kg of body wt./day, could reduce the number of leukocytes and mast cells and thereby expedite the healing of incisional wounds in mice. This reduction is probably due to the phenolic compounds present in the basil with anti-inflammatory properties.

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References

1 Nguyen AV & Soulika AM, The Dynamics of the Skin´s Immune System. *Int J Mol Sci*, 20 (2019) 1811.

2 Sevilla A, Chéret J, Slominski RM, Slominski AT & Paus R, Revisiting the role of melatonin in human melanocyte physiology: A skin context perspective. *J Pineal* Res, 72 (2022) e12790.

3 Kim Y & Lim KM, Skin barrier dysfunction and filaggrin. *Arch Pharm Res*, 44 (2021) 36.

4 Kim H, Kim DE, Han G, Lim NR, Kim EH, Jang Y, Cho H, Jang H, Kim KH, Kim SH & Yang Y, Harnessing the Natural Healing Power of Colostrum: Bovine Milk-Derived Extracellular Vesicles from Colostrum Facilitating the Transition from Inflammation to Tissue Regeneration for Accelerating Cutaneous Wound Healing. *Adv Health Mater*, 11 (2022) 2102027.

5 Huang C, Dong L, Zhao B, Lu Y, Huang S, Yuan Z, Luo G, Xu Y & Qian W, Anti-inflammatory hydrogel dressings and skin wound healing. *Clini Transl Med*, 12 (2022) e1094.

6 Khezri K, Farahpour MR & Rad SM, Efficacy of *Mentha pulegium* essential oil encapsulated into nanostructured lipid carriers as an *in vitro* antibacterial and infected wound healing agent. *Colloids Surf A Physicochem Eng Asp*, 589 (2020) 124414.

7 Kant V, Sharma M, Jangir BL & Kumar V, Acceleration of wound healing by quercetin in diabetic rats requires mitigation of oxidative stress and stimulation of the proliferative phase. *Biotech Histochem*, 97 (2022) 461.

8 Mathew-Steiner SS, Roy S & Sen CK, Collagen in Wound Healing. *Bioengineering*, 8 (2021) 63.

9 Rodrigues M, Kosaric N, Bonham CA & Gurtner GC, Wound Healing: A Cellular Perspective. *Physiol Rev*, 99 (2019) 665.

10 Wang ZC, Zhao WY, Cao Y, Liu YQ, Sun Q, Shi P, Cai JQ, Xiao Z, Shen XZ & Tan WQ, The Roles of Inflammation in

Keloid and Hypertrophic Scars. *Front Immunol*, 11 (2020) 603187.

11 Tessema Z, & Molla Y, Evaluation of the wound healing activity of the crude extract of root bark of *Brucea antidysentrica*, the leaves of *Dodonaea angustifolia* and *Rhamnus prinoides* in mice. *Heliyon*, 7 (2021) e05901.

12 Okur ME, Karadağ AE, Özhan Y, Sipahi H, Ayla Ş, Daylan B, Kültür Ş, Demirci B & Demirci F, Anti-inflammatory, analgesic and *in vivo-in vitro* wound healing potential of the *Phlomis rigida* Labill. extract. *J Ethnopharmacol*, 266 (2021) 113408.

13 Yaldiz G, Camlica M, Pradhan Y & Ali A, Chemical Characterization, Biological Activities, and Some Medicinal Uses of Different Sweet Basil (*Ocimum basilicum* L.) Genotypes.*Nat Prod Experiment Drug Discovery*, (2022) 41.

14 Dhama K, Sharun K, Gugjoo MB, Tiwari R, Alagawany M, Iqbal YM, Thakur P, Iqbal HNM, Chaikumpa W, Michalack I, Elnesr SS & Farag MR, A comprehensive review on chemical profile and pharmacological activities of *Ocimum basilicum*. *Food Rev Int*, 39 (2023) 119.

15 Kamelnia E, Mohebbati R, Kamelnia R, El-Seedi HR & Boskabady MH, Anti-inflammatory, immunomodulatory and anti-oxidant effects of *Ocimum basilicum* L. and its main constituents: A review. *Iranian J Basic Med Sci*, 26 (2023) 617.

16 Qasem A, Assaggaf H, Mrabti HN, Minshawi F, Rajab BS, Attar AA, Alyamani RA, Hamed M, Mrabti NN, Baaboua AE, Omari NE, Alshahrani MM, Awadh AAA, SheiKh RA, Ming LC, Goh KW & Bouyahya A, Determination of Chemical Composition and Investigation of Biological Activities of *Ocimum basilicum* L. *Molecules*, 28 (2023) 614.

17 Eftekhar N, Moghimi A, Hossein BM, Kaveh M & Shakeri F, *Ocimum basilicum* affects tracheal responsiveness, lung inflammatory cells and oxidant-antioxidant biomarkers in sensitized rats. *Drug Chem Toxicol*, 42 (2019) 286.

18 Aye A, Jeon YD & Lee JH, Anti-inflammatory activity of ethanol extract of leaf and leaf callus of basil (*Ocimum basilicum* L.) on RAW 264.7 macrophage cells. *Orient Pharm Exp Med*, 19 (2019) 217.

19 Zangeneh MM, Zangeneh A, Seydi N & Moradi R, Evaluation of cutaneous wound healing activity of *Ocimum basilicum* aqueous extract ointment in rats. *Comp Clin Pathol*, 28 (2019) 1.

20 Kmail A, Jaradat N, Mansour B, Abu-Labdeh R, Zakarneh S, Abu-Farha S, Hussein F, Issa L & Saad B, Phytochemical analysis, cytostatic, cytotoxic, and anti-inflammatory effects of *Arum palaestinum*, *Ocimum basilicum*, and *Trigonella foenum-graecum* in human monocytic cell line (THP-1)-derived macrophages. *Eur J Integr Med*, 54 (2022) 102159.

21 Bejeshk MA, Aminizadeh AH, Rajizadeh MA, Khaksari M, Lashkarizadeh M, Shahrokhi N, Zahedi MJ & Azimi M, The effect of combining basil seeds and gum Arabic on the healing process of experimental acetic acid-induced ulcerative colitis in rats. *J Tradit Complement Med*, 12 (2022) 599.

22 Zhang Y, He H, Wang D, Song L & He C, Evaluation of *in vitro* anti-acne activities of Ocimum basilicum L. water extract. *Ind Crops Prod*, 186 (2022) 115205.

23 Anusmitha KM, Aruna M, Job JT, Narayanankutty A, Benil PB, Rajagopal R, Alfarhan A & Barcelo D, Phytochemical analysis, antioxidant, anti-inflammatory, anti-genotoxic, and anticancer activities of different Ocimum plant extracts prepared by ultrasound-assisted method. *Physiol Mol Plant Pathol*, 117 (2022) 101746.

24 Kumari M, Prasad A, Mathur A, Mathur AK, Ur-Rahman L, Singh M& Lal RK, Precursors and elicitor induced enhancement of cell biomass and phenolic compounds in cell suspensions of Indian basil-*Ocimum basilicum* (CIM-Saumya). *Physiol Mol Biol Plants*, 29 (2023) 679. https://doi.org/10.1007/s12298-023-01316-6.

25 Beheshti F, Vakilian A, Navari M, Zare MM, Dinpanah H & Ahmadi-Soleimani SM, Effects of *Ocimum basilicum* L. Extract on Hippocampal Oxidative Stress, Inflammation, and BDNF Expression in Amnesic Aged Rats. *Exp Aging Res*, (2023) 1. doi: 10.1080/0361073X.2023.2210240.

26 Araújo SG, Lima WG, Pinto MEA, Morais MÍ, de Sá NP, Johann S & dos Santos Lima LAR, Pharmacological prospection in-vitro of Lamiaceae species against human pathogenic fungi associated to invasive infections. *Biocatal Agric Biotechnol*, 21 (2019) 101345.

27 Araújo SG, Amado PA, Pinto MEA, Castro AHF & Lima LDS, Total phenol and antioxidant potential of five species of Lamiaceae family. *Period Tchê Química*, 16 (2019) 239.

28 Araújo SG, Alves LF, Pinto MEA, Oliveira GT, Siqueira EP, Ribeiro RIMA, Ferreira JMS & Lima LARS, Volatile compounds of Lamiaceae exhibit a synergistic antibacterial activity with streptomycin. *Braz J Microbiol*, 45 (2014) 1341.

29 Mehraein F, Sarbishegi M & Aslani A, Evaluation of effect of oleuropein on skin wound healing in aged male BALB/c mice. *Cell J*, 16 (2014) 25.

30 Mahmood SAA & Sidik K, Synergistic effects of alcoholic extracts of sweet Basil (*Ocimum basilicum* L.) leaves and honey on cutaneous wound healing in rats. *Int J Mol Med Adv Sci*, 1 (2005) 220.

31 Wulff BC, Parent AE, Meleski MA, DiPietro LA, Schrementi ME & Wilgus TA, Mast cells contribute to scar formation during fetal wound healing. *J Invest Dermatol*, 132 (2012) 458.

32 Komi DEA, Khomtchouk K & Santa MPL, A review of the contribution of mast cells in wound healing: involved molecular and cellular mechanisms. *Clin Rev Allerg Immunol*, 58 (2020) 298.

33 Sun K, Li YY & Jin J, A double-edged sword of immuno-microenvironment in cardiac homeostasis and injury repair. *Signal Transduct Target Ther*, 6 (2021) 79.

34 Bacci S, Fine regulation during wound healing by mast cells, a physiological role not yet clarified. *Int J Mol Sci*, 23 (2022) 1820.

35 Dong J, Chen L, Zhang Y, Jayaswal N, Mezghani I, Zhang W & Veves A, Mast cells in diabetes and diabetic wound healing. *Adv Ther*, 37 (2020) 4519.

36 Xu X, Zeng Y, Chen Z, Yu Y, Wang H, Lu X, Zhao J & Wang S, Chitosan-based multifunctional hydrogel for sequential wound inflammation elimination, infection inhibition, and wound healing. *Int J Biol Macromol*, 235 (2023) 123847.

37 Xu Z, Liang B, Tian J & Wu J, Anti-inflammation biomaterial platforms for chronic wound healing. *Biomater Sci*, 9 (2021) 4388.

38 Rodrigues LB, Martins AOBPB, Ribeiro-Filho J, Cesário FRAS, Castro FE, de Albuquerque TR, Fernandes MNM, da Silva

BAF, Quintans Júnior LJ, Araújo AAS, Menezes PDP, Nunes PS, Matos IG, Coutinho HDM, Goncalves Wanderley A & de Menezes IRA, Anti-inflammatory activity of the essential oil obtained from *Ocimum basilicum* complexed with β-cyclodextrin (β-cd) in mice. *Food Chem Toxicol*, 109 (2017) 836.

39 Shahrajabian MH, Sun W & Cheng Q, Chemical components and pharmacological benefits of Basil (Ocimum basilicum): A review. *Int J Food Prop*, 23 (2020) 1961.

40 Romano R, De Luca L, Aiello A, Pagano R, Di Pierro P, Pizzolongo F & Masi P, Basil (Ocimum basilicum L.) leaves as a source of bioactive compounds. *Foods*, 11 (2022) 3212.

41 Pandey AK, Tiwari SP, Biswas D, Patel Y, Jajda HM & Dave GS, Evaluation of Phytochemicals, Antioxidant and Anti-inflammatory properties of leaves of *Ocimum basilicum* L. *Res J Pharm Technol*, 16 (2023) 1981.

42 Tian D, Yang Y, Yu M, Han ZZ, Wei M, Zhang HW, Jia HM & Zou ZM, Anti-inflammatory chemical constituents of Flos Chrysanthemi Indici determined by UPLC-MS/MS integrated with network pharmacology. *Food Funct*, 11 (2020) 6340.

43 Kim HP, Son KH, Chang HW & Kang SS, Anti-inflammatory plant flavonoids and cellular action mechanisms. *J Pharmacol Sci*, 96 (2004) 229.

44 Osei Akoto C, Acheampong A, Boakye YD, Naazo AA & Adomah DH, Anti- Inflammatory, Antioxidant, and Anthelmintic Activities of Ocimum basilicum (Sweet Basil) *Fruits J Chem*, 2020 (2020) 1.

45 Ambreen M& Mirza SA, Evaluation of anti-inflammatory and wound healing potential of tannins isolated from leaf callus cultures of Achyranthes aspera and Ocimum basilicum. *Pak J Pharm Sci*, 33 (2020) 361.