

The effect of 3% passion fruit purple variant (*Passiflora edulis Sims var. Edulis*) seed extract cream on facial skin aging

Medina Muslim, Nelva Karmila Jusuf*, Imam Budi Putra*

Postgraduate Master of Clinical Medicine Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Universitas Sumatera Utara Hospital, Medan, Indonesia.

* Department of Dermatology and Venereology, Faculty of Medicine Universitas Sumatera Utara, Universitas Sumatera Utara Hospital, Medan, Indonesia.

Abstract

Background Facial skin aging is a progressive, multifactorial and complex processes that greatly affects appearance so many people try to postpone this process. In North Sumatra, the passion fruit purple variant (*Passiflora edulis Sims var. edulis*) is commonly planted. Piceatannol, ascorbic acid, flavonoids, resveratrol, and sterols found in industrial waste seeds play a role in alleviating the appearance of skin aging via antioxidant, anti-inflammatory, tyrosinase inhibition, promoting fibroblast proliferation, and collagen formation. The objective of this study was to determine the effect of 3% passion fruit purple variant seed extract cream on facial skin aging.

Methods This pre-experimental clinical trial study was conducted on 40 participants with facial skin aging. History and clinical evaluation utilizing the Dermoscopic Photoaging Scale (DPAS) following administration of 3% passion fruit purple variant seed extract cream at baseline, weeks 2, 4, 6, and 8 validated the diagnosis. All adverse effects were documented during the course of the trial, and participant satisfaction was evaluated at week 8. Statistical analysis using repeated Anova test was done to evaluate the differences before and after intervention, with $p < 0.05$ denotes statistical significance.

Results There were significant decrease in DPAS score in participants with facial skin aging ($p=0.000$) after 8 weeks of using passion fruit purple variant seed extract cream. Only 1 out of 40 participants (2.5%) experienced adverse effects of mild and transient dry skin. Most of the participants (82.5%) indicated good satisfaction level.

Conclusion Topical use of 3% passion fruit purple variant seed extract cream can improve the appearance of facial skin aging with minimal adverse effects and good satisfaction level.

Key words

Facial skin aging; Passion fruit seed extract: DPAS; Antioxidant.

Introduction

Skin aging is a progressive, multifaceted, and complicated process that alters the skin's appearance, structure, mechanism, and function. Additionally, the skin serves as a social interface between individuals. Since the skin is the key to someone's identity, many people are pursuing anti-aging treatments for the skin, particularly facial skin.¹⁻³ The clinical and histological

findings on adults and the elderly who have been exposed to the sun for an extended period of time on their skin exhibit are referred to as

Address for correspondence

Dr. Medina Muslim

Department of Dermatology and Venereology,
Faculty of Medicine Universitas Sumatera Utara,
Universitas Sumatera Utara Hospital, Medan,
Indonesia.

Ph: +62 85262561615

Email: medinaamuslim@gmail.com

photoaging, also known as premature skin aging. The presence of wrinkles, rough skin, telangiectasias, discolored skin, patchy pigmentation, and various benign, premalignant, and even malignant neoplasms are all signs of photoaging.^{4,6} UV light affects the skin's collagen matrix by promoting matrix metalloproteinase (MMP)-mediated collagen breakdown and suppressing procollagen synthesis. In photoaged skin, the balance of MMP-1 and type I procollagen expression is crucial. It has been hypothesized that photoaged and naturally aged skin exhibit wrinkles as a result of collagen deficiency or alteration.^{3,7,8}

Social behavior and reproductive status may be positively affected by a young and appealing look, which opens the way for further research into so-called "anti-aging products." Many topical agents have been used to treat the appearance of aging skin.⁹ The use of sunscreens, retinoids, and antioxidants is believed to enhance the appearance of aging skin.¹⁰ In topical formulations, antioxidants from a broad number of vitamins, provitamins, such as vitamin E, vitamin C, coenzyme Q10, and phenolic compounds from plant extracts can prevent or treat clinical manifestations of skin aging, such as chronological aging and photoaging.^{10,11}

Due to their abundant availability in nature, encouraging results, and low adverse effects, natural resource antioxidants have become increasingly popular in recent years. The efficacy of polyphenolic chemicals found in numerous natural plants, such as tropical fruits, has been intensively researched, with the majority of studies focusing on its advantages for skin health. Free radicals, inhibits the oxidation process, absorbs UV rays, and suppresses enzymatic activity. This mechanism occurs because of the alleged presence of phenolic compounds in it.^{12,13}

Antioxidants, polyphenols are chemical compounds found in a variety of plants. Passion fruit seeds have been found to contain a lot of polyphenols, the most important of which is piceatannol (4, 4, 3', 5'-tetrahydroxy-trans-stilbene).¹⁴ It is well known that piceatannol has many benefits for the skin, including increasing the production of collagen, decreasing the production of melanin, increasing the antioxidant activity of glutathione, and eliminating the formation of reactive oxygen species (ROS).¹⁵

Matsui *et al.* reported that *Passiflora edulis* has an inhibitory effect on melanogenesis and stimulates collagen synthesis. The high level of polyphenol in *Passiflora edulis* seed extract can inhibit tyrosinase activity. This will contribute to the prevention of skin damage and aging.¹⁶ Follow-up studies also reported a considerable reduction in melanin production after application of purple passion fruit extract to melanoma cell cultures at a concentration of 20µg/mL and a substantial increase in collagen synthesis at a concentration of 200µg/mL.¹⁴

Maruki-Uchida *et al.* in their study of 32 women aged 35-54 years in Japan showed that *Passiflora edulis* seed extract containing piceatannol 5 mg for 8 weeks, significantly increased skin moisture and reduced transepidermal water loss. Piceatannol is thought to play a role in the production of collagen, the inhibition of melanin synthesis, the production of glutathione antioxidants, and the elimination of free radicals.¹⁵ In line with this study, it was reported that 6% passion fruit purple variant seed extract cream might make striae distensae look better.¹⁷ The purpose of this study is to determine the effect of 3% passion fruit purple variant seed extract cream on facial skin aging.

Methods

Study design and ethical concerns This pra

experimental one group pretest-posttest design clinical study was conducted from July 2021 until April 2022 at the Outpatient Clinic Department of Dermatology and Venereology, Universitas Sumatera Utara General Hospital, Indonesia. The Research Ethics Committee of Universitas Sumatera Utara, Indonesia approved the protocol of this study (Grant Number No. 949/KEP/USU/2021). Written informed consent was obtained from each participant before enrollment.

Subjects and intervention The participants were comprised of 40 women aged 30–55 years, who attended the Outpatient Clinic Department of Dermatology and Venereology, Universitas Sumatera Utara General Hospital, Indonesia with facial skin aging. All participants were evaluated for dermatological history and examination. Participants were not included in this study if they had any dermatoses which may interfere with facial skin aging changes, had previous history of allergic to facial cosmetic products, were previously treated with topical retinoids and its derivatives, antioxidants, vitamin C, vitamin E in one month prior to the study, were previously treated with oral retinoids, antioxidants, vitamin C, vitamin E in the one month prior to the study, perform regular facial skin rejuvenation treatments such as chemical peeling, microneedling, dermabrasion and microdermabrasion, botulinum toxin or filler injection and various light and laser therapies within the last three months of the study, using contraceptives that contain estrogen or hormone replacement therapy, have undergone plastic surgery and or reconstructive surgery procedures on the face, was menopause, pregnant and/or breastfeeding.

After cleaning the facial skin with a gentle cleanser two times daily, all participants applied 1 finger tip unit of 3% passion fruit purple variant seed extract cream symmetrically across

their entire face day and night. Participants were asked to avoid excessive sun exposure and use sunscreen regularly. Participants were eliminated from the trial if they did not apply the cream for three days in a row or if they applied it for fewer than seven weeks in total and if they used oral, topical antiaging facial skin products or underwent procedures for facial skin rejuvenation during the study period.

Plant material, extraction and formulation of topical cream The passion fruit purple variant in this study was cultivated in Brastagi, North Sumatera, Indonesia. Prior to extraction, the seeds were isolated from their pulps, dried at 40°C, and pulverized into simplicia using a blender. The 3% passion fruit purple variant seed extract cream was prepared at Laboratorium ASPETRI Medan.

Outcome evaluation The demographic data were collected initially, including identity and age. The effect was measured using changes in participants' *Dermoscopic Photoaging Scale* (DPAS) score. Four facial regions were evaluated using a Dermlite DL3N (3Gen, Inc., California, United States): the forehead, right malar, left malar, and chin.¹⁸ Yellowish discoloration, yellow papules, white lines (skin atrophy), ephelides/ lentigines, hypo-hyperpigmented macules, telangiectasia, actinic keratoses, senile comedones, superficial wrinkles, deep wrinkles, and crisscross wrinkles were identified as photoaging signs according to DPAS. Every 2 weeks (weeks 2, 4, 6 and 8), participants were asked to come back for an assessment of the DPAS score, adverse effects that occurred, the level of satisfaction of the participant during the study period and documentation. Each participant underwent dermoscopic photography in the same condition carried out by one person. At each visit, a dermatology resident assessed any remaining potential adverse effects and documented any

potential adverse effects that participants had recorded between sessions.

Statistical analysis SPSS software was used to analyze the data. All data gathered during weeks 0, 2, 4, 6, and 8 were assessed using the Saphiro–Wilk test for normality. To compare DPAS scores at the end of treatment to those at baseline, the repeated ANOVA test was applied, and a P value of less than 0.05 was considered statistically significant. The number of participants and percentages were used to determine adverse effects and satisfaction level.

Results

Forty participants were enrolled in the study, and each of them fulfilled it. The mean±SD age of participants was 39.45±5.93 years and a large number of participants (40%) belonged to the 35-39 year old age group. The demographic profile for participants is shown in **Table 1**.

Initial mean DPAS score at baseline was 13.15±4.023. After 8 weeks of applying passion fruit purple variant seeds extract cream, the DPAS score decreased significantly to 10.52±3.83. The results of the study demonstrated that 3% passion fruit purple variant seed extract cream can result in clinically and statistically significant improvements in facial skin aging (**Figure 1**). A significant decline was observed in the mean±SD DPAS score following the treatment ($P < 0.05$) (**Table 2**).

Table 1 Demographic data based by age.

Age (years)	n	%
30-34	7	17.5
35-39	16	40
40-44	10	25
45-49	4	10
50-55	3	7.5
Total	40	100

Table 2 Difference in DPAS scores before and after the application of 3% passion fruit purple variant (*Passiflora edulis Sims var. edulis*) seeds extract cream.

Period of study	n	DPAS Score Mean ± SD	P value*
Baseline	40	13.15 ± 4.023	
2 nd Week	40	13.10 ± 3.999	
4 th Week	40	12.77 ± 4.117	0.000
6 th Week	40	11.27 ± 4.273	
8 th Week	40	10.52 ± 3.83	

Table 3 Patients satisfaction levels.

Satisfaction level	n	%
None	0	0
Minimal	0	0
Moderate	4	10
Good	33	82.5
Very good	3	7.5
Total	40	100

The only adverse event that occurred was mild and transient dry skin in one participant. In completion of the study, participants were requested to report their level of satisfaction based on the improvement in their facial skin condition. Eighty-two point five percent of the participant expressed a good satisfaction level (**Table 3**).

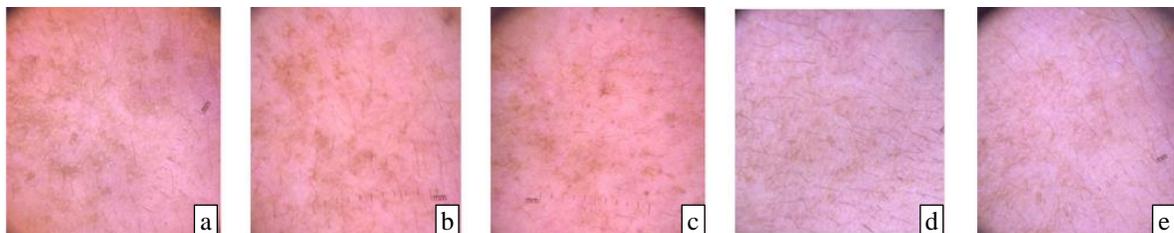


Figure 1 Improvement of the appearance of facial skin aging by using 3% passion fruit purple variant (*Passiflora edulis Sims var. edulis*) seed extract cream. Baseline (week 0) (a); after 2 weeks (b); after 4 weeks (c); after 6 weeks (d); after 8 weeks (e).

Discussion

In parallel with the advancement of medical technology, Isik *et al.* developed DPAS as a quantitative noninvasive examination scale to evaluate facial skin aging. DPAS has a score of 0 to 44 which is assessed based on 11 criteria that can be found on aging facial skin. These criteria include yellowish discoloration, white lines, lentigines, hypopigmented-hyperpigmented macules, telangiectasis, yellow papules, actinic keratoses, senile comedones, superficial wrinkles, deep wrinkles, and criss-cross wrinkles.¹⁸ In week 0 observations, the mean DPAS value was 13.15 ± 4.023 .

This cohort prospective study indicates that 3% passion fruit purple variant seed extract cream can enhance the presence of facial skin aging through DPAS which decreased the mean value from week 0 of 13.15 ± 4.023 to 10.52 ± 3.83 at week 8. This may develop as a result of the content of piceatannol, ascorbic acid, flavonoids, resveratrol, sterols and other alkaloid groups in purple passion fruit seeds.^{14,19,20}

Polyphenols are regarded as a natural antioxidant. It has been proved that polyphenols exhibit antioxidant properties towards skin cells. Excessive formation of free radicals is caused by exposure to UV light, stress, medications, and numerous other environmental factors. Numerous studies have discovered that passion fruit purple variant could be a valuable source of natural antioxidants that can neutralize or suppress the activity of free radicals, hence supporting the body in maintaining optimal antioxidant levels.²¹ Piceatannol, the main polyphenolic compound in passion fruit seeds, has been shown to have the highest antioxidant capacity in the Ferric Reducing Antioxidant Power (FRAP) assay when compared to fruit pulp and skin. Passion fruit seeds are rich in polyphenolic compounds.²² The antioxidant

activity of piceatannol exerts a positive effect on the formation and regeneration of skin cells.²³ Furthermore, the administration of *Passiflora edulis* seeds extract to diabetic rats induced by streptozotocin led to an increase in enzymatic antioxidants in visceral organs.^{21,24}

Passiflora edulis seed extract inhibited melanogenesis and promoted collagen synthesis, according to Matsui *et al.* The high polyphenol content in *Passiflora edulis* seed extract can inhibit tyrosinase activity.¹⁶ After applying purple passion fruit seed extract to melanoma cell culture at a concentration of 20 $\mu\text{g/mL}$, a 2013 follow-up study found a substantial reduction in melanin synthesis.¹⁴ Maruki-Uchida *et al.* in their study in Japan showed that *Passiflora edulis* seed extract containing piceatannol 5 mg significantly increased skin moisture and decreased transepidermal water loss. This is thought to be related to piceatannol's role in stimulating collagen production, suppressing melanin synthesis, inducing antioxidant glutathione, and eliminating free radicals.¹⁵

Numerous in vivo tests have been used to determine *Passiflora edulis* extract's anti-inflammatory properties. *Passiflora edulis* leaf extract was found to lower IL-1b and TNF levels in mice subjected to 2, 4, 6-trinitrobenzenesulphonic acid-induced colitis in an animal study. In the meantime, it is known that the peel reduces the expression of TNF, IL-1b, IL-6, IL-12, and IL-17, which are proinflammatory cytokines.^{25,26} Montaher *et al.* reported the effect of *Passiflora edulis* extract as an anti-inflammatory which was evaluated by measuring myeloperoxidase and nitric oxide levels in pleurisy patients. In this procedure, *Passiflora edulis* inhibited myeloperoxidase and nitric oxide levels more effectively than dexamethasone (0.5 mg/kg) ($p < 0.01$).^{27,28} The presence of an alkaloid group in *Passiflora*

edulis has also been shown to exhibit significant anti-inflammatory activity with inhibits the NF- κ B signaling pathway.²²

In addition to having a strong antioxidant and anti-inflammatory mechanism, *Passiflora edulis* seed extract also contributes to the improvement fibroblast proliferation and epithelialization as well as inducing collagen synthesis.²⁹ This was revealed by in vitro experiments of flavonoid administration in fibroblast culture, which led to a major increase in collagen synthesis compared to placebo.^{30,31} The delivery of passion fruit purple variant extract at a dosage of 200 μ g/mL to melanoma cell cultures was likewise associated with a significant increase in collagen synthesis.¹⁴

The aging process has been the subject of more than a dozen hypothesized explanations, including the free radical theory, the immunological theory, the inflammatory theory, and the mitochondrial damage theory. To explain the changes associated with the aging process, each theory provides a distinct cause of aging. Despite the fact that scientists examine each theory independently, the aging process is a continuous process that is synergistically interrelated to each other.^{1,32} Inflammation and the increase in free radicals are among the main theories in the skin aging process. *Passiflora edulis* has antioxidant, anti-inflammatory properties and plays a role in increasing collagen synthesis, fibroblast proliferation and epithelialization, so it has potential as an antiaging skin agent. Findings that have been described previously support the findings of this study which demonstrate the ability of passion fruit purple variant extract cream to be beneficial in improving the appearance of facial skin aging.

No adverse reaction in the form of redness, swelling, desquamation, itching, or burning was observed. Mild and transient dry skin occurs in

one participant at the first week after cream application. Majority of the participants stated a good satisfaction level. It is possible to draw the conclusion that the administration of passion fruit purple variant seeds extract topically results in a high level of satisfaction and a low risk of adverse effects on facial skin aging.

A number of limitations need to be considered in this study. This study is the preliminary study to determine the effect of 3% passion fruit purple variant seed extract in cream preparations, so it is still not known which ingredients can cause irritation, besides that it is not clear about the interaction between the ingredients contained in the vehicle and the extract. The results of this study provide a basis for further investigation regarding the clinical use of passion fruit purple variant seed extract, especially for skin health. In the future, studies with a larger number of participants with randomized and controlled study designs need to be carried out.

Conclusion

According to the findings of this study, the passion fruit purple variant seed extract cream can reduce the signs of facial aging. Only one participant experienced minor, brief adverse effects. As indicated by the degree of fulfilment, most of participants were satisfied during the use of 3% natural product purple variation seed extract cream. To compare this extract's safety and efficacy to the standard treatment for facial skin aging, additional prospective studies are required.

References

1. Ganceviciene R, Liakou AI, Theodoridis A, Zouboulis CC, Ganceviciene R, Liakou AI, et al. Skin anti-aging strategies. *Dermatoendocrinol.* 2012;1980.
2. Jusuf NK. Kulit Menua. *Majalah Kedokteran Nusantara* [Internet]. 2005;38(2):184–9. Available from:

- [http://repository.usu.ac.id/bitstream/123456789/15569/1/mkn-jun2005-\(7\).pdf](http://repository.usu.ac.id/bitstream/123456789/15569/1/mkn-jun2005-(7).pdf)
3. Assaf H, Adly M, Hussein M. Aging and Intrinsic Aging; Pathogenesis and Manifestations. In: Farage MA, Miller KW, Maibach HI, editors. *Textbook of Aging Skin*. USA: Springer; 2010. p. 130–318.
 4. Ansari U, Harvey VM. Other effects of ultraviolet light: photosensitivity, photoreactivity and photoaging. In: Li BS, Maibach HI, editors. *Updates in Clinical Dermatology: Ethnic Skin and Hair and Other Cultural Considerations* [Internet]. Switzerland: Springer Nature; 2021. p. 55–70. Available from: <http://www.springer.com/series/13203>
 5. Mohiuddin AK. Skin Aging & Modern Age Anti-aging Strategies. *Glob J Med Res*. 2019;**19**(2):15–60.
 6. Huang AH, Chien AL. Photoaging: a Review of Current Literature. *Curr Dermatol Rep*. 2020;**9**(1):22–9.
 7. Jusuf NK. Broccoli flower extract (*Brassica oleracea* L. var.italica plenck) inhibits photoaging by increasing type I procollagen expression in human skin fibroblast. *Int J Pharmtech Res*. 2016;**9**(3):114–8.
 8. Jusuf NK, Bachtiar A, Hadisahputra S, Soebono H. Effect of Broccoli Flower Extract (*Brassica oleracea* L. var. italica Plenck) on Inhibition of Photoaging Viewed from Matrix Metalloproteinase-1 Expression in Human Skin Fibroblast. *J Biol Agric Healthc*. 2014;**4**(26):54–9.
 9. Baumann L, Saghari S. Photoaging. In: Baumann L, Saghari S, Edmund W, editors. *Cosmetic Dermatology*. Second Edi. United States: Mc Graw Hill; 2009. p. 34–41.
 10. Minkis K, Swary JH, Alam M. Photoaging. In: Draelos Z, editor. *Cosmetic Dermatology Products and Procedures*. Second. UK: Wiley Blackwell; 2016. p. 13–22.
 11. Sekar M. Rambutan fruits extract in aging skin [Internet]. 2nd ed. Aging. Elsevier Inc.; 2020. 303–307 p. Available from: <http://dx.doi.org/10.1016/B978-0-12-818698-5.00031-6>
 12. Pouillot A, Polla LL, Tacchini P, Neequaye A, Polla A, Polla B. Natural Antioxidants and their Effects on the Skin. *Formulating, Packaging, and Marketing of Natural Cosmetic Products*. 2011;239–57.
 13. Masaki H. Role of antioxidants in the skin: Anti-aging effects. *J Dermatol Sci* [Internet]. 2010;**58**(2):85–90. Available from: <http://dx.doi.org/10.1016/j.jdermsci.2010.03.003>
 14. Matsui Y, Sugiyama K, Kamei M, Takahashi T, Suzuki T, Katagata Y, *et al*. Seeking a new anti-skin-aging material: Piceatannol and its derivatives from passion fruit (*Passiflora edulis*) seed. *ACS Symposium Series*. 2013;**1129**:189–202.
 15. Hiroko M, Minoru M, Yoshikazu Y, Masahiko S. Effect of Passion Fruit Seed Extract Rich in Piceatannol on the Skin of Women : A Randomized , Placebo-Controlled , Double-Blind Trial. *J Nutr Sci Vitaminol*. 2018;**75**–80.
 16. Matsui Y, Sugiyama K, Kamei M, Takahashi T, Suzuki T, Katagata Y, *et al*. Extract of passion fruit (*Passiflora edulis*) seed containing high amounts of piceatannol inhibits melanogenesis and promotes collagen synthesis. *J Agric Food Chem*. 2010;**58**(20):11112–8.
 17. Aryunisari CG, Putra IB, Jusuf NK. Effect of purple passion fruit extract cream (*Passiflora edulis* sims var. *edulis*) 6% against striae distensae. *Open Access Maced J Med Sci*. 2021;**9**:720–5.
 18. Isik B, Gurel MS, Erdemir AT, Kesmezacar O. Development of skin aging scale by using dermoscopy. *Skin Research and Technology*. 2013;**19**(2):69–74.
 19. Ramaiya SD, Bujang JS, Zakaria MH, King WS, Shaffiq Sahrir MA. Sugars, ascorbic acid, total phenolic content and total antioxidant activity in passion fruit (*Passiflora*) cultivars. *J Sci Food Agric*. 2013;**93**(5):1198–205.
 20. Wulandari R, Sari RM, Yani YP, Tjong DH. Genetic Variation in Purple Passion Fruit (*Passiflora edulis* f. *edulis* Sims.) in West Sumatra, Indonesia by RAPD Markers Genetic Variation in Purple Passion Fruit (*Passiflora edulis* f. *edulis* Sims.) in West Sumatra , Indonesia by RAPD Markers. 2017;(July).
 21. He X, Luan F, Yang Y, Wang Z, Zhao Z, Fang J, *et al*. *Passiflora edulis* : An Insight Into Current Researches on Phytochemistry and Pharmacology. *Frontiers in Pharmacology*. 2020;**11**:1–16.
 22. Morais DR, Rotta EM, Sargi SC, Schmidt EM, Guntendorfer E, Eberlin MN, *et al*. Antioxidant activity , phenolics and UPLC–ESI(–)–MS of extracts from different tropical fruits parts and processed peels. *FRIN* [Internet]. 2015; Available from:

- <http://dx.doi.org/10.1016/j.foodres.2015.08.036>
23. Yockteng R, Coppens G, Souza-chies TT, Leo PC de. Passiflora. In: Kole C, editor. Wild Crop Relatives: Genomic and Breeding Resources. Berlin: Springer; 2011.
 24. Kelly J, Baú C, Cazarin B, Colomeu TC, Giovana Â, Meletti LMM, *et al.* Antioxidant activity of aqueous extract of passion fruit (*Passiflora edulis*) leave: In vitro and in vivo study. *Food Research International*. 2013;**53**:882–90.
 25. Baú C, Cazarin B, Kelly J, Cristina T, Giovana Â, Maria L, *et al.* Intake of *Passiflora edulis* leaf extract improves antioxidant and anti-inflammatory status in rats with 2, 4, 6-trinitrobenzenesulphonic acid induced colitis. *J Funct Foods* [Internet]. 2015;**17**:575–86. Available from: <http://dx.doi.org/10.1016/j.jff.2015.05.034>
 26. Garrido-mesa J, Guerra-hernández E, Aparecida P, Braga DC, Guillermo F, Reyes R, *et al.* Intestinal anti-inflammatory effects of *Passiflora edulis* peel in the dextran sodium sulphate. *J Funct Foods* [Internet]. 2016;**26**:565–76. Available from: <http://dx.doi.org/10.1016/j.jff.2016.08.020>
 27. Beatriz A, Maria S, Paulo E, Fr S. Evidence of anti-inflammatory effects of *Passiflora edulis* in an inflammation model. *J Ethnopharmacol*. 2007;**109**:281–8.
 28. Montanher AB, Zucolotto SM, Schenkel EP, Fröde TS. Evidence of anti-inflammatory effects of *Passiflora edulis* in an inflammation model. *J Ethnopharmacol*. 2007;**109**(2):281–8.
 29. Gonçalves Dias Filho A, Torres OJM, Campos ACL, Tâmbara Filho R, Rocha LCDA, Thiede A, *et al.* Effect of *Passiflora edulis* (passion fruit) extract on rats bladder wound healing: Morphological study. *Acta Cir Bras*. 2006;**21**(UPPL. 2):1–6.
 30. Soares RDF, Campos MGN, Ribeiro GP, Salles BCC, Cardoso NS, Ribeiro JR, *et al.* Development of a chitosan hydrogel containing flavonoids extracted from *Passiflora edulis* leaves and the evaluation of its antioxidant and wound healing properties for the treatment of skin lesions in diabetic mice. *J Biomed Mater Res A*. 2020; **108**(3):654–62.
 31. Stipcevic T, Piljac J, Berghe D vanden. Effect of different flavonoids on collagen synthesis in human fibroblasts. *Plant Foods for Human Nutrition*. 2006;**61**(1):29–34.
 32. Fibrich BD, Lall N. Fighting the inevitable: Skin aging and plants [Internet]. Medicinal Plants for Holistic Health and Well-Being. Elsevier Inc.; 2017. 75–115 p. Available from: <https://doi.org/10.1016/B978-0-12-812475-8.00003-2>.