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Snakehead Fish Extract in Increasing Skin Collagen & Fibroblasts

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Abstract: This study aim is to gain a deeper understanding of the mechanisms by which snakehead fish extract affects the skin, opening doors for the development of more effective and natural skincare products. The study employs a systematic literature review method using PRISMA strategy, identifying 156 relevant articles through platforms such as PubMed, Google Scholar, Scopus, SINTA, spanning from 2018 to 2023. Findings encompass increased VEGF production and NO levels with snakehead fish extract dosages, wounds healing potential of honey and snakehead fish skin combination in hydrogel formulations, increased fibroblast counts, reduced skin erythema, and decreased wound crust formation. Additionally, marine collagen exhibits promise in skin healing and bone repair. Collagen supplements, whether oral or topical, also prove beneficial in delaying skin aging. The study reveals crucial insights into the potential of snakehead fish extract in skincare and wound healing, supporting the development of more effective and natural skincare products.

Keywords: Collagen Production; Skin Fibroblast; Snakehead Fish Extract

Introduction

Collagen and fibroblasts are the two main components in maintaining skin health and elasticity. Collagen is a structural protein that provides strength and flexibility to skin tissue, while fibroblasts are the cells responsible for collagen production. Both play an important role in maintaining a youthful and wrinkle-free appearance of skin. The extracted snakehead fish is a natural source of fatty acids, collagen protein, omega-3, and various other important nutrients, and has long been used in traditional medicine to improve skin health. However, in-depth scientific research into its effects on collagen production and skin fibroblast activity is still limited (Nasution et al., 2020). So the following study investigates the potential of extracted snakehead fish in renewing collagen production and skin fibroblast activity, as well as to identify the specific ingredients in extracted snakehead fish that contribute to these benefits (Maretalinia et al., 2023; Sukmawati, 2018). A deeper understanding of the mechanism of action of extracted snakehead fish on the skin, this research can pave the way for the development of more effective and natural skin care products.

In addition, this research also supports efforts to identify natural resources that have potential as active ingredients in the environmentally friendly skin care industry. Snakehead fish, often overlooked in this context, has great potential to be a more sustainable alternative to the synthetic chemicals often used in skin care products. Utilizing existing natural resources, we can reduce negative impacts on the environment while promoting sustainable use in the cosmetics and skin care industry.

The contents of snakehead fish that have a positive impact on collagen and skin fibroblasts include omega-3 fatty acids, type I and III collagen proteins, not forgetting vitamin E, vitamin C, and zinc. Omega-3 fatty acids are known to have anti-inflammatory properties and are able to maintain the integrity of skin cells. Type I and III collagen proteins are the main components in the skin structure and can stimulate more collagen production. Meanwhile, the role of vitamin C is as a substitute for collagen and zinc has antioxidant properties which provide a shield for skin cells damaged by free radicals. Further research will help us

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understand the role of each of these components in improving skin health and allow the development of more advanced skin care products based on natural resources (Tungadi, 2019; Umage et al., 2020).

Combining scientific knowledge about the potential of snakehead fish with the increasing consumer need for natural and sustainable skin care, this research is an important first step in developing skin care products that are effective, environmentally friendly and based on local natural resources. In conclusion, research on extracting snakehead fish that increases collagen and skin fibroblast activity not only provides new insight into the skin health benefits of this natural ingredient but also has the potential to encourage innovation in the skin care industry for a moresustainable and beneficial future for human skin health (Hendriati et al., 2019).

Because basically everyone wants healthy and attractive skin. However, as we age, our skin ages due to physiological changes. Reactive oxygen species (ROS) arethe main pathogenic components in human aging. Human skin is susceptible to ROS produced by both extrinsic sources such as ultraviolet (UV) radiation from the sun andinternal oxidative metabolism. The collagen-rich extracellular matrix (ECM) is damaged by ROS-mediated oxidative stress, which is characteristic of aging skin connective tissue. Damage to the dermal collagen ECM reduces the structural integrity of the skin and produces an abnormal tissue environment that promotes age-related skindiseases such as poor wound healing and the development of skin cancer (Tu et al., 2016). The result of collagen degradation in the skin is the appearance of signs of aging such as wrinkles and loss of elasticity. Collagen is a structural protein found in the layers of the skin, and functions to provide strength, firmness and elasticity to the skin. When collagen degrades or decreases in production with age or due to environmental factors, such as excessivesun exposure or smoking, the skin loses its structure.

The use of collagen supplements to slow down the aging process has become a force in the field of beauty, especially cosmetics and dermatology therapy. According to research, tropical and oral types of collagen are often used for aging treatment. All human studies included in randomized controlled trials, most of which were conducted in high- to middle-income countries, found that oral and topical collagen supplements helped slow the aging process, with no difference between the two forms of collagen. When used orally, both collagen supplements improve skin moisture, elasticity, and hydration. Additionally, collagen improves wrinkles and skin roughness, and previous studieshave identified no negative side effects from taking it orally (Al-Atif, 2022).

The Channidae family, which is a related group of 26 types of fish, apparently shows great diversity throughout Asia with 23 types holding their own parties. However, when we glance into the stomachs of the Channidae fish that enjoy life in Indian waters, the world oftheir taxonomy and phylogeny seems like an unopened fog.This cutting-edge research carried out a thorough investigation of eight celebrities from Chann's world. Gene sequence analysis turned up two distinct groups that seemed to be at two ends of the genetic galaxy, and interestingly, they displayed identical levels of phylogenetic clarity. A piece of the genetic story of these two genes can provide quite a different puzzle to identify these eight Channaspecies (Lakra et al., 2010).

A number of studies have been conducted to examine the potential of extracted snakehead fish to increase collagen production and skin fibroblast activity. First, research by Xiu et al. (2018) showed that extracting snakehead fish contains omega-3 fatty acids which can stimulate collagen production and improve skin elasticity (Xu et al., 2021). Second, Oslan et al. (2022) found that snakehead fish that underwent extraction contained type I and III collagen proteins which can increase collagen production in skin cells (Oslan et al., 2022). Third, research by Ginta (2020) reveals that snakehead fish that have undergone extraction contain vitamin C which can help in collagen synthesis (Ginta, 2020). Fourth, research by Awuchi et al. (2022) highlightedthe anti-inflammatory properties of omega-3 fatty acids in extracted snakehead fish which can reduce skin damage dueto inflammation (Awuchi et al., 2022). Fifth, research by Lim et al. (2019) explored the potential of extracting snakehead fish to inhibit the activity of enzymes that damage collagen, maintaining skin collagen density (Lim et al., 2019).

Overall, these findings show the great potential of extracted snakehead fish in improving skin health and treating signs of aging. However, while the initial evidenceis compelling, it is important to note that much of this research is still in its early stages and requires further extensive and in-depth research, including clinical trials in humans, to more concretely validate its benefits. Nevertheless, extracted snakehead fish offers potential as a promising natural ingredient in the development of future skin care products that are more effective and sustainable.

There are several research gaps that need to be considered to develop further research on Snakefish that undergo extraction to increase collagen and skin fibroblast activity. One significant research gap is the lack of in- depth study of the molecular mechanisms behind how extracted snakehead fish interacts with skin cells to stimulate collagen production and fibroblast activity. More specifically, this research can focus on

identifying the biochemical pathways involved in the effects of snakehead fish undergoing extraction at the molecular level.

The novelty of future research could include a deeper understanding of the specific components in extracted snakehead fish that have the effect of stimulating collagen and fibroblast activity. This includes identifying the active compounds responsible for these benefits. Furtherresearch can also test various doses of snakehead fish that undergo extraction to determine the optimal dose to improve skin health. Additionally, there is potential to conduct larger and longer clinical studies in human populations to validate laboratory findings and measure thelong-term effects of extracting snakehead fish on human skin.

Apart from a scientific perspective, it is also important to study the impact of snakehead fish undergoing extraction on environmental sustainability and ethics in the use of natural resources. Developing more environmentally friendly extraction methods and sustainable management practices for snakehead fish resources could be an important part of this research.

Overall, research gaps and novelties in future research should focus on a deeper understanding of the mechanisms, active components, optimal dosage, and impact of using extracted snakehead fish in the context of healthy, effective, and sustainable skin care.

Method

A systematic literature review with the PRISMA strategy to identify research relevant to the theme "Snakefish that underwent extraction in increasing collagen and skin fibroblast activity" was used in the research. Data was found through the journal platforms PubMed, Google Scholar, Scopus, SINTA, and all known data totaled 156. This data was then filtered by random selection to select the research most relevant to this research topic, with the time period from 2018 to 2023 as a reference . After selection, 15studies were selected that met these criteria. The selected data is then reduced and classified based on the author's name, year of publication, research methods used, and research results achieved.

Next, in the data analysis stage, the author interprets the findings of the selected research. The aim is to carry out inductification from the data presented in the research. Thus, this research not only collects informationfrom relevant sources, but also links these findings into a more comprehensive framework of understanding. Analysis of this data is the basis for further discussion about the potential of extracted snakehead fish in increasing collagenand skin fibroblast activity as well as understanding research gaps that need to be filled in future research

Result and Discussion

Discussion

The fatty acid content in the muscles of these fish was analyzed to reveal their nutritional value. In this regard, cyprinid fish muscle stands out because it has a significant content of long-chain omega-3 polyunsaturated fatty acids (LC-PUFA) compared to fish from the families Channidae and Cobitidae. Noting unexpectedly, fish such as snakehead fish, which are known as carnivorous predators, have lower levels of LC-PUFA compared to fishthat tend to be detritivores or herbivores. This indicates that the content of omega-3 polyunsaturated fatty acids (PUFA) in fish muscles varies in line with their eating habits. Although it is commonly recommended to consume marinefish as the main source of omega-3 PUFA for health, the benefits of consuming freshwater fish remain, especially since some species contain significant amounts of beneficial omega-3 PUFA.

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Not only wounds, but snakehead fish also play a role in increasing fibroblast cells. In the data it has been

stated that there is research from (Atmajaya et al., 2019). The copper mineral contained in this ingredient plays an important role in stimulating the production of fibroblast growth factor (FGF), which in turn triggers an increase in the number of fibroblast cells in the body. Meanwhile, zinc(Zn) and copper (Cu) also have a crucial role in binding and optimizing the activity of the superoxide dismutase (SOD) enzyme, which functions to reduce inflammation that may occur during the healing process. In addition, the iron content in this ingredient supports oxygen transport and promotes collagen synthesis which is necessary in the wound healing process. Thus, these minerals make a significant contribution in supporting the health and healingof the human body.

Table 1. Literature Review

Author & year of publication	Research methodology	Results
Nasution et al (2020)	Study experiment ation	Snakehead fish that underwent extraction significantly increasedVEGF levels as the dose increased, with the highest levelsoccurring in Group P3 (361.7 ± 40.2; p < 0.001). NO levels also increased with increasing dosesof snakehead fish that underwent extraction, with the highest NO levels occurring in Group P3 (59.43 ± 0.88 µmol/gr; p < 0.001). VEGFR2 expression also increased significantly after administration of snakehead fish that underwent extraction alongwith increasing doses (p<0.001), where administration of 800 mg of extract resulted in the highest expression of VEGFR2 comparedto lower doses (17.7 vs. 15.6; p<0.001).
Ismail et al (2023)	arrative review	Honey has antioxidant,antimicrobial and anti-inflammatory characteristics which can modulate the immune system, while snakehead fish skinis rich in protein, minerals and collagen which supports a faster wound healing process. When combined in a hydrogel formulation, these two ingredients have the potential to work together to accelerate burn wound healing.
Taslim et al (2022)	Experimen tation test	A significant increase in the number of fibroblasts on day 3 ofthe group given snakehead fish that underwent extraction. Significant changes are not sharply visible.
Geahchan et al (2022)	Exploratory review	Marine collagen is a very versatile compound capable of healing skin injuries of varying degrees of severity, as well as slowing down the natural human aging process. Marine collagenhas been proven to be able to trigger keratinocyte and fibroblast
Ramadhanti et al (2021)	Experimental laboratory	A trend was found to decrease the average number of macrophages and blood vessels in treatment group 1 and treatment group 2. There was a significant differencebetween the control group and treatment group 2, but there was no significant difference betweenthe other groups.
Kwan et al (2019)	FDWE, SDWE, MTT, andring test.	The samples showed a positive reaction in cell growth and the formation of new blood vessels. There are four important proteins/genes identified, namelycollagen type XI, actin 1, and myosin light and heavy chains. Connected with these proteins, important pathways were found such as the integrin pathway, Slit-Robo signaling, and immune responses via CC Chemokine Receptor-3 on eosinophils, whichplay a role in wound healing mechanisms.
Perera et al (2020)	Literacyreview	In this study, there were six species of snakehead fish that were officially recognized, namely C. marulius, Channa ara, C. kelaartii, C. orientalis, C. punctata, and C. striata. However,a recent review shows that understanding of the phylogeny and geographic distribution of theChannidae family in Sri Lanka remains incomplete, and identifies several areas of deficiency that need to be emphasized in future research.
Truong et al (2021)	Experimental test	This study shows that collagen can be isolated effectively from snakehead fish remains and has potential as a realistic alternative to mammalian collagen.
Baehaki et al (2020)	xperimental study	The results showed that the hydrolysis time treatment had a significant effect on the degree ofhydrolysis (13.98% - 27.08%), with a peptide content of 2.73% -3.78% and antioxidant activity of10.75% - 20. 7%. The results of the degree of hydrolysis show thatthe longer the hydrolysis time, thepercentage of degree of hydrolysis will increase. Peptide content and antioxidant activity also increased with increasing hydrolysis time.

Author & year of publication	Research methodology	Results
Tungadi (2019)	Experimental study	The results showed that the hydrolysis time treatment had a significant effect on the degree of hydrolysis (13.98% - 27.08%), with a peptide content of 2.73% -3.78% and antioxidant activity of10.75% - 20. 7%. The results of the degree of hydrolysis show that the longer the hydrolysis time, thepercentage of degree of hydrolysis will increase. Peptide content and antioxidant activity also increased with increasing hydrolysis time.
Sun et al (2023)	Genomic analysis, gene knockdow n experiments, and transcripto mic analysis	The results showed that the YM snakehead fish is an albino with total loss of melanin in the skin and eyes, which is inherited as a recessive Mendelian trait. The research also identified a non- sense genetic mutation in the slc45a2 gene as the cause of the YM snakehead phenotype. In addition, it was found that YM snakehead fish had higher melanogenesis gene expression levels and signaling pathways such as MAPK, WNT, and calcium were also more active. These pathways may be responsible for the increased production of elements of melanogenesis and are likely influenced by fibroblast-derived melanogenic factors in a paracrine mechanism.
Jaya-Ram et al (2018)	Experimental laboratory	The results of the study showed that the fatty acid content in the muscles of cyprinids (Java lampam and river lampam) was higher compared to fish and the Channidae and Cobitidae families. The content of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are the highest types of omega-3 fatty acids, was recordedin the muscles of river lampam and Javan lampam. On the other hand, haruan fish, which are predators, have lower LC-PUFA content compared to fish with detrivor/herbivore characteristics.
(Nugroho, 2022)	Control group at post-test	The results showed that the ALP level in odontoblast cells exposedto haruan fish extract added with calcium hydroxide increased compared to the control group. This increase occurred at various extract concentrations, namely 25µg/ml = 208.37 µg/ml, 50 µg/ml = 219.04 µg/ml, and 100 µg/ml = 282.93 µg/ml, and was significantly different from the control group.

Based on a number of practicums that have been carried out, There are several interesting explanations regarding the potential of snakehead fish (Channa striata) as a skin healing agent in mammals. This snakehead fish contains significant levels of albumin, a protein that is important in the formation of new cells and tissue. In this experiment, white mice were divided into three groups, with one group being a negative control that was given emulgel base, one group being a positive control that received povidone-iodine, and another group being given emulgel containing snakehead fish that had undergone 10% extraction. On the third and seventh days, white mice were sacrificed for microscopic observation. Extracted snakehead fish emulgel accelerates wound healing in white mice by increasing fibroblast cells and collagen This snakehead fish contains significant levels of albumin, a protein that is important in the formation of newcells and tissue.

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Channa striata fish, which is rich in bioactive proteins, was tested to accelerate wound healing using twodifferent extracts. The results showed that these two extracts stimulated cell proliferation and pro-angiogenic activity. This study identified four essential proteins,such as collagen type (Kwan et al., 2019).

Extracted snakehead fish has been proven to be effective in accelerating the healing of stage II acute wounds with a concentration of 20% being the most effective. Research also reveals that polyunsaturated fatty acids (PUFA), such as eicosapentaenoic and docosahexaenoic, can increase the production of proinflammatory cytokines at the wound site, providing potential as a noninvasive therapy to influence skin wound healing (Daisa et al., 2017; McDaniel et al., 2008).

Testing of the effect of snakehead fish on the healing of perineal wounds, which can be caused by tears during childbirth or episiotomy procedures, has been carried out. The slow healing process of perineal wounds can increase susceptibility to infection, so it is important to ensure an adequate supply of nutrients, especially protein, to support the proliferation of new cells during this healingstage. The results of statistical analysis using the Mann- Whitney test showed that there was a significant differencein the effectiveness of perineal wound healing between thegroup that received egg white intake and the group that was given snakehead fish extract as treatment. Morespecifically, Consuming egg whites was proven to be significantly more efficient in accelerating the healing process of perineal wounds compared to the group that received snakehead fish extract treatment. These findings provide valuable insight in the context of postnatal care, highlighting the critical role of certain nutrients in facilitating faster and more efficient healing of perineal wounds (Purnani, 2019).

Gel extract derived from snakehead fish (Channa striatus) apparently outperforms mackerel gel extract in thecontext of accelerating the wound healing process after tooth extraction in white rat subjects. The results of rigorousstatistical analysis confirmed that the albumin activity of chitosan nanoparticles derived from extracted snakehead fish, which has its origins in the natural habitat of Kalimantan, produced a significant positive impact in accelerating the wound healing process after tooth extraction when compared with the control group that did not receive similar treatment. This indicates the potential use of extracted snakehead fish in the context of wound healing therapy and highlights its effectiveness in improving the tissue healing process after tooth extraction in white rats (Prayugo et al., 2021; Utami et al., 2020).

There are things that actually act as supporting substances for the substances contained in the snakehead fish itself as a healer for the skin because of the presence ofanti-oxidants. As in research (Ismail et al., 2023). Researchconducted by Ismail et al. in 2023 highlighting the importance of supporting substances in snakehead fish as skin healers, especially through their antioxidant role. Thisstudy shows that snakehead fish contains large amounts of antioxidants which can play an important role in the skin healing process. Antioxidants are compounds that help protect skin cells from damage caused by free radicals and oxidative stress. The presence of antioxidants in snakehead fish can help reduce inflammation, stimulate the growth of fibroblast cells, and support collagen synthesis which is needed in wound healing. Therefore, snakehead fish not only contains important nutrients such as albumin, amino acids, fatty acids and minerals, but also antioxidants whichcan help speed up the skin healing process.

Through the data that has been supported by this discussion, it can be seen that snakehead fish with all its contents has the ability to stimulate collagen production and the growth of fibroblast cells. The nutritional content such as albumin, amino acids, fatty acids, and minerals such as copper (Cu) and zinc (Zn) in snakehead fish play a role in supporting the skin and tissue healing process. In addition, the antioxidants in snakehead fish also help protect skin cells from oxidative damage, which is an important component in the healing process. All of this illustrates thepotential of snakehead fish as a valuable natural source in stimulating collagen formation, fibroblast cell growth, and supporting optimal skin healing. A deeper understanding ofthe role of snakehead fish in the tissue healing process,

The potential of snakehead fish in stimulating collagen formation and fibroblast cell growth also provideshope in the development of skin care products and nature- based healing therapies. Utilizing the natural healing properties of snakehead fish, such as increased collagen production and natural antioxidants, researchers and skin care product developers can create more effective formulasto treat skin problems, including wounds, skin damage, andsigns of aging. In addition, further research may reveal more specific ways to isolate and optimize important componentsin snakehead fish

that contribute to skin healing.

Therefore, snakehead fish is not only part of local culinary culture, but also a valuable resource in the field of health care and skin beauty. Its ability to increase collagen formation and support the growth of fibroblast cells makes it a promising natural ingredient for the development of more natural, safe and effective skin care products. It is hoped that future research can explore this potential more deeply and maximize the benefits of snakehead fish in theworld of skin care and health.

Conclusion

Snakehead fish (Channa striata) and its extracts have great potential in supporting the healing process involving collagen and fibroblast cell growth. Extracted snakehead fish have been shown to increase the level of the enzyme alkaline phosphatase (ALP) in MDPC-23 odontoblast cells, which is an indication of increased osteogenesis activity and collagen synthesis, which are important in healing bone and tooth tissue.

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Investigation, M.F.S and I.G.N.D; formal analysis, , M.F.S and I.G.N.D; investigation, , M.F.S and I.G.N.D; resources, M.F.S and I.G.N.D; data curation, , M.F.S and I.G.N.D: writing—original draft preparation, , M.F.S and I.G.N.D ; writing—review and editing, , M.F.S and I.G.N.D: visualization, , M.F.S and I.G.N.D; supervision, , M.F.S and I.G.N.D; project administration, , M.F.S and I.G.N.D; funding acquisition, , M.F.S and I.G.N.D. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest
We certify that there is no conflict of interest with any financial, personal and other relationships with other peoples or organization related to the material discussed in the manuscript

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