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# Fish Skin Graft as Wound Dressing to Provide Acceleration of Wound Healing: A Narrative Review

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**Abstract:- Acellular fish skin grafts (FSGs) are tissue-based products derived from the minimally processed skin of the Atlantic cod (Gadus morhua). The FSG has a high amount of omega-3 fatty acids, which aid in the regeneration of tissues by promoting the growth of new blood vessels and tissue formation throughout the stages of wound healing known as proliferation and remodeling. FSG exhibits a higher degree of structural resemblance to human skin compared to antiviral-treated skin substitutes like amniotic membrane. Furthermore, there is no evidence of any prion, bacterial, or viral infections being transmissible from North-Atlantic cod to humans. The FSG undergoes proprietary processing that maintains the integrity and lipid composition of the skin. FSG is presently the sole acellular dermal matrix product that does not derive from mammalian tissues. This review will examine the efficacy of FSG as a wound dressing.**

***Keywords:-*** *Fish skin Graft, Wound Dressing, Regeneration.*

## I. INTRODUCTION

Skin grafts are frequently employed to aid in the closure of nonhealing wounds, which demand substantial healthcare resources and pose a serious public health concern due to their high morbidity and substantial expenses. Grafts can be acquired from the patient themselves (autograft), a human donor (allograft), or from different species (xenograft). Kerecis created a xenograft in 2013 using the skin of the Atlantic cod (Gadus morhua). Kerecis Omega3 Wound is a decellularized fish skin graft (FSG) that is used to treat several types of wounds such as traumatic wound, burned skin, decubitus ulcer, and diabetic ulcers. The FSG sheet comprises lipids, proteins, elastin, glycans, and other inherent constituents of the skin, with a notable abundance of omega-3 fatty acids. These features ensure a superior integration compared to human allograft, supported by statistically validated evidence. The acellular FSG's advanced cellularization process and distinctive biomechanical features make it an optimal choice for serving as a protective covering for severe trauma and burn wounds in military combat situations. Moreover, the authors delineated the antibacterial properties of FSG, which enable it to resist bacterial infiltration for a duration of 48-72 hours.[1]

Various methods can be employed to heal wounds, taking into account their depth and the level of damage. These methods include, but are not limited to, the use of collagen alginate dressings, silver sulfadiazine cream 1%, autografts, allografts, and xenografts. A collagen alginate dressing is a sterile dressing that has a high concentration of collagen. It creates a moist environment for wounds, which helps promote the growth of new tissue and speeds up the healing process. The primary purpose of using Silver sulfadiazine cream 1% is to establish a protective barrier between a wound and its surroundings. Additionally, it possesses antibacterial qualities that facilitate the process of re-epithelization and wound healing. Autografts are skin grafts that are harvested from a different, uninjured area of the body of the same individual with the wound. Allografts refer to skin grafts obtained from a donor who is a distinct individual, while xenografts are skin transplants obtained from animals such as pigs, cattle, or fish. These grafts are referred to as cellular and/or tissue-based products (CTP).[2,3]

The aim of this review is to discuss the benefit of fish skin graft in skin reconstruction field.

## II. ACUTE AND CHRONIC COMPLEX WOUND

Approximately 1%–2% of the population in affluent countries is projected to encounter a chronic illness at some point in their lives. The management of CW is a formidable challenge for surgeons due to the arduous and protracted healing process, the adverse effects on quality of life, and the substantial financial burden they entail. Currently, there is no universally accepted treatment documented in the literature for these types of lesions. Multiple debridement approaches are accessible, including surgical, biosurgical, and enzymatic methods, as well as VAC and acellular dermal matrix. Kirsner et colleagues conducted a comparative analysis of the impact of FSG and human amniotic membrane on acute full-thickness tissue injury. A double-blind, prospective randomised trial demonstrated that FSG is markedly more effective than human amniotic membrane in terms of healing time for acute wounds.[4] The hazard ratio of 2.37 (95% CI: 1.75–3.2, P = 0.001) further supports this finding. In a double-blinded randomised controlled trial. Baldursson et colleagues examined the healing duration of biopsy wounds treated with FSG (Kerecis Omega-3 Wound) compared to swine small intestinal submucosa extracellular matrix. A total of 82 patients were included in the study. The group treated with FSG showed a significantly faster healing at 28 days, with a statistically significant difference (P = 0.041). Furthermore, no notable statistically negative

response was observed, and there was no indication of the development of autoantibodies. Badois et al suggested employing FSG (Full-thickness Skin Graft) for treating the superficial wounds at the donor site in patients who underwent free flap reconstructions for head and neck cancer. Twenty-one patients were divided into two groups by the researchers: group 1 had paraffin gauze treatment as normal care, whereas group 2 received FSG treatment. When employing the fish skin matrix in place of the conventional wound care protocol, the statistical analysis revealed a significant ($P < 0.05$) reduction in the number of local infections and pain, but at a greater cost for the FSG.[5] Dorweiler et al used the Kerecis Omega3 wound to treat 21 patients with complicated diabetes-related limb wounds showing how FSG stimulates the granulation tissue and reepithelialization as well as having antibacterial and analgesic effects.[7]

Ciprandi et al documented their observations in the juvenile population, specifically focusing on different types of lesions (including six trauma-related, two autoimmune disease-related wounds, three cases of surgical dehiscence, and four sacral ulcer wounds). The patients in this study received treatment with FSG to achieve complete wound closure. A portion of the posttraumatic injuries were a result of animal bites, a prevalent occurrence in the field of pediatrics. The authors of the article reported that all patients experienced fast wound healing, with the whole wound area being covered and complete healing achieved in 95% of cases. The study also demonstrated the significant impact of negative pressure wound therapy, with the average duration of application being reduced by half, from the typical 21 days to an average of 12 days. Consequently, they determined that FSG is an inventive and enduring remedy for treating wounds in children, leading to decreased surgical duration and hospital stays, along with faster wound healing.[8] The study conducted by Yang et al. involved 18 patients who had full-thickness ulcers that were either larger than 20 $cm^2$ or had been present for a minimum of 52 weeks. The researchers employed the FSG (Fragrance Sensory Group) and conducted an examination of the scent, discharge, state of the nearby skin, presence of redness, and any negative effects. They then compared these findings to the use of typical extracellular matrices. The researchers determined that the FSG appears to be a promising and successful method for sealing wounds in conjunction with extracellular matrices.[9]

## III. DIABETIC FOOT

The global prevalence of diabetes stands at roughly 10.8% of the total population, while the projected incidence of developing diabetic foot is expected to be around 6.3% in the year 2023. Wound management solutions typically involve active treatments like vacuum-assisted closure (VAC) and skin grafts, or passive treatments such as acellular dermal matrices. If a skin graft is required, the novel FSG could serve as a viable alternative. Woodrow et al conducted a study on eight patients who received FSG treatment for the treatment of diabetic foot wounds after surgery. The study shown that fish skin was well tolerated and has the ability to effectively speed up the healing process of the wounds.[9] Lullove et al examined the healing rate of index ulcers and the time it took for ulcers to heal in diabetic foot patients. They compared the use of FSG with the standard of care, which involved using collagen alginate dressing. Their findings indicated a notable disparity in the percentage of cured wounds after 12 weeks between the bigger groups, with the FSG group demonstrating superior performance compared to the SOC group. Zehnder et al administered standard of care (SOC) and fibrin sealant glue (FSG) to all venous and diabetic lesions. The researchers administered FSG treatment to patients who did not exhibit a decrease in the affected area above 50% within a 4-week period. Out of the total of 42 patients, 21 required FSG treatment. This indicates that patients who underwent FSG treatment experienced a minimum improvement of 25% compared to standard of care (SOC) in terms of the time required to achieve complete healing. Additionally, they noted that the cost was equal for both therapies, despite the fact that patients who received fish skin grafting required a shorter duration of treatment.[10,11]

## IV. BURNS

As per the World Health Organization, burns pose a worldwide public health issue, resulting in almost 180,000 fatalities each year. Effectively managing burns poses a significant challenge for both patients and healthcare practitioners. For deep dermal and full-thickness burn injuries, the recommended primary treatment is prompt removal of damaged tissue and the use of partial-thickness skin grafts (STSGs). This approach aims to close the wound quickly and prevent common issues like infections, unsightly scarring, and incomplete healing. Nevertheless, in the case of extensive burns, the availability of autologous skin becomes a concern. Surgeons frequently depend on allogenic and xenogeneic skin, sourced from human cadavers and pig skin, to provide temporary coverage after removing the damaged tissue. Recently, FSG has become increasingly popular in this domain because to its attributes, including its ability to prevent infection, alleviate pain, and promote swift healing of wounds. In their study of 10 patients, Alam et al utilized FSG (Full-Thickness Skin Graft) for treating full-thickness burn injuries. They described FSG as an outstanding, strong, and flexible xenograft that was simple to administer. Consequently, based on the restricted patient population, they determined that the observed pain-relieving impact and the relatively brief duration until complete reepithelialization were encouraging. FSG acts at the molecular level by creating an extracellular matrix made up of glycosaminoglycans, proteoglycans, fibronectin, and growth factors. This matrix helps in the movement of cells from the patient's own body, so improving the stages of cell growth and the formation of new skin in the healing process of burns.[12,13]

## V. COMPARISON WITH OTHER GRAFTS PRODUCTS

In 2019, Lima Junior et al. conducted a randomized control experiment to assess the effectiveness of AFS grafts compared to silver sulfadiazine cream 1% in treating superficial partial thickness burns. The study comprised a cohort of 30 pediatric patients, aged two to 12 years, who were hospitalized for superficial partial thickness burns that had transpired over the past 72 hours. The wounds of both groups were cleansed using water and a solution containing 2% chlorhexidine gluconate. Anesthesia, either with or without midazolam, was administered using ketamine during the initial dressing. A total of 15 patients in the experimental group underwent the application and bandaging of an AFS graft. If the AFS graft failed to adhere properly to the wound, it was replaced. The AFS graft was only excised upon the manifestation of complete re-epithelialization. The control group, consisting of 15 patients, received treatment with a 1% silver sulfadiazine cream and underwent daily dressing changes. The disparity in mean duration for complete re-epithelialization between the two groups was not statistically significant. The test group had an average of 10.07 ± 0.46 days, whereas the control group had an average of 10.47 ± 0.74 days. Upon removal of the dressing, the extent of wound healing was assessed in both groups, revealing a notable improvement compared to the initial stage of treatment.[14]

In 2020, Winters et al. performed a retrospective comparative cohort research to assess the cost-effectiveness of using AFS grafts compared to collagen alginate dressings for treating DFUSs. The study included 59 diabetic foot ulcers (DFUs) in 55 patients. Two similar hypothetical cohorts were formed: one cohort treated the wounds with AFS grafts, while the other cohort treated them with collagen alginate dressing. The models were subsequently compared. The analysis demonstrated that the expense associated with each DFU treatment utilizing AFS grafts amounted to $11,210, whereas wounds treated with collagen alginate dressing had a cost of $15,075. The utilization of AFS grafts resulted in a greater incidence of wound healing and a reduced occurrence of amputations. Overall, the utilization of AFS grafts presents a more economically efficient approach in managing DFUs, while also yielding superior healing results for individuals.[15]

## VI. CONCLUSION

The literature analysis revealed that the utilization of fish skin grafts for treating diabetic foot ulcers (DFUs) and burn wounds is more effective compared to other alternative wound dressing techniques. The exceptional biochemical characteristics of AFS make it an optimal option for the treatment of chronic and acute superficial and deep partial thickness wounds. The current research provides valuable assistance to wound care specialists by presenting a contemporary and economical alternative that has demonstrated outstanding results. This alternative has the potential to benefit both developed nations and economically disadvantaged ones.

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