

# WHAM evidence summary: fish skin for treating burns

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## CLINICAL QUESTION

What is the best available evidence for fish skin for treating burns?

## SUMMARY

In low and middle resource settings, fish skin has been used as a low cost, traditional biological dressing for treatment of burns and other wounds. The high collagen concentration and tensile strength<sup>1-4</sup> of fish skin has led to its use as a xenograft. There is insufficient clinical evidence on healing outcomes to make a recommendation on using fish skin for treating burns. *Level 1* evidence<sup>5-7</sup> at high risk of bias suggests that complete healing might be faster with a fish skin dressing compared to the local standard care (most frequently, silver sulfadiazine cream replaced every two days), but the time to healing difference was negligible in most studies and may not be clinically significant. *Level 1* evidence<sup>5-7</sup> on effectiveness in achieving better control of pain intensity showed mixed results. However, no studies reported that fish skin dressings were inferior to local standard care, adverse events were not reported to be an issue and some low level evidence indicated people receiving fish skin dressings were satisfied with the outcomes.

## CLINICAL PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional and the clinical context.

There is insufficient evidence to make a recommendation on the use of fish skin dressings to promote healing in burns.

## SOURCES OF EVIDENCE: SEARCH AND APPRAISAL

This summary was conducted using methods published by the Joanna Briggs Institute.<sup>8-11</sup> The summary is based on a systematic literature search combining search terms related to fish skin, burns and healing. Searches were conducted for evidence reporting use of fish skin in human burns published

up to 31 January 2024 in English in the following databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline (Ovid), Google Scholar, Embase (Ovid), AMED, Global Health, Health Internetwork Access to Research Initiative (Hinari, access via Research4Life) and Cochrane Library. Levels of evidence for intervention studies are reported in Table 1.

## BACKGROUND

Some types of fish skin have been used as a wound dressings in low resource communities due to their similarities to human skin. Fish skin has high collagen concentration, high resistance, and high tensile strength.<sup>1-4</sup> Fish skin also has antiviral, anti-bacterial and anti-oxidative properties, and is rich in unsaturated fatty acids, which might contribute to efficacy as a burn treatment.<sup>4,16</sup>

The clinical research in this evidence summary is focused on the use of natural fish skin that is applied directly to burns (usually after a sterilisation process). The fish skin adheres to the wound bed as a xenograft, protecting the wound bed during healing and reducing the number of dressing changes that are required. This has potential to reduce healthcare resources and to reduce wound-related pain.<sup>1,2,4,5,12,15</sup>

Bench research has also described the extraction and use of collagen from fish skin in commercial wound dressing products, including sponges, hydrogels and topical powders<sup>3,17-22</sup> but no clinical research on the use of these products for human burns was identified in the literature search.

## CLINICAL EVIDENCE ON FISH SKIN FOR WOUND HEALING

Studies reporting clinical outcomes for human burns treated with tilapia fish skin dressing and shaour fish skin dressing are summarized in Table 2. Half of the published evidence<sup>1,2,6,7</sup> was produced by one team in Brazil.

### Fish skin for promoting healing in burns

The highest level of evidence comes from a meta-analysis<sup>5</sup> at high risk of bias that included three studies<sup>1,6,7</sup> (reported below). Pooled results showed tilapia fish skin dressing was associated with shorter time for partial-thickness burns to reach complete epithelialisation (standard mean difference [SMD] -0.903, 95% confidence interval [CI] -1.45 to -0.355,

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$p < 0.001$ ) (Level 1). The primary studies all showed positive outcomes for healing with fish skin dressings:

- One RCT<sup>7</sup> at moderate risk of bias, compared tilapia fish skin dressing with silver sulphadiazine 1% cream for treating partial thickness burns. The study had three arms based on the depth and extent of the participants burns (arm A: superficial second-degree burns to less than 10% of the body [n = 23]; arm B: superficial second-degree burns to 10–20% of the body [n = 19] and arm C: deep second-degree burns to 5–15% of the body [n = 20]). After light debridement and cleansing with a topical antimicrobial, the treatment group in each arm received a tilapia fish

skin dressing, gauze and a bandage. Every 48 hours the secondary dressing was removed to check the fish skin dressing was correctly adhered. The control group in each arm received the local standard care regimen (silver sulphadiazine 1% cream, gauze and a bandage, changed every 48 hours). In all three study arms, complete epithelialisation was achieved significantly faster in burns treated with the tilapia fish dressing (mean difference between treatment arm and control arm ranged from 1.43 to 3.20 days,  $p < 0.05$  in all arms)<sup>7</sup> (Level 1).

- In an RCT<sup>6</sup> at high risk of bias the same research team extended their research in individuals with partial thickness

Table 1. Levels of evidence for clinical studies

Level 1 evidence	Level 2 evidence	Level 3 evidence	Level 4 evidence	Level 5 evidence
<b>Experimental designs</b>	<b>Quasi-experimental designs</b>	<b>Observational – analytic designs</b>	<b>Observational – descriptive studies</b>	<b>Expert opinion/ bench research</b>
1.b Systematic review of RCTs and other study designs <sup>5</sup>  1.c Randomised controlled trial <sup>6,7</sup>	2.c Quasi-experimental prospectively controlled study <sup>12</sup>	3.e Observational study with control group <sup>13</sup>	4.c Case series <sup>4</sup>  4.d Case study <sup>1,2,14</sup>	5.a Narrative literature review <sup>15-17</sup>  5.c Bench research <sup>3, 18-22</sup>

Table 2. Summary of the primary evidence for tilapia fish skin dressing for wound management

Study	Country	Tilapia fish treatment and comparators (number wounds)	Type of wounds	Wound outcome measures	Level of evidence
Alam et. al. (2019) <sup>4</sup>	UK	Nile tilapia fish skin and dry gauze (n = 12)	Split skin graft donor sites (n = 10) Partial thickness burns (n = 2)	Signs of local infection Number of days to 90% and 100% epithelialisation Pain intensity	4
Costa et. al. (2019) <sup>2</sup>	Brazil	Nile tilapia fish skin, dry gauze and bandage (n = 1)	Superficial partial-thickness burns	Time to 100% epithelialisation	4
Kotkot et. al. (2022) <sup>13</sup>	Yemen	Shaour fish skin and dry gauze (n = 18)	Superficial and deep partial-thickness burns	Signs of local infection Number of days to 90% and 100% epithelialisation Pain intensity	3
Lima Júnior et. al. (2020) <sup>7</sup>	Brazil	Nile tilapia fish skin, gauze and bandage (n = 32) Silver sulphadiazine 1% cream, gauze and bandage (n = 30)	Superficial and deep partial-thickness burns	Time to 100% epithelialisation Pain intensity	1
Lima Júnior et. al. (2021) <sup>6</sup>	Brazil	Nile tilapia fish skin, gauze and bandage (n = 57) Silver sulphadiazine 1% cream, gauze and bandage (n = 58)	Partial-thickness burns	Time to 100% epithelialisation Pain intensity	1
Lima Júnior et. al. (2019) <sup>1</sup>	Brazil	Nile tilapia fish skin, silver sulphadiazine 1% cream, gauze and bandage (n = 1)	Partial-thickness burns	Time to 100% epithelialisation	4
Putri et. al. (2022) <sup>12</sup>	Indonesia	Nile tilapia fish skin, gauze and bandage (n = 4) Paraffin-impregnated gauze, gauze and bandage (n = 4)	Full thickness burns	Bates-Jensen Wound Assessment Tool (BWAT)	2

burns. Individuals with burns to up to 10% of the body that occurred no more than 72 hours prior and had not yet received treatment were eligible for the trial if they had no product sensitivity or significant co-morbidities. The treatment and control dressing regimens were the same as in the RCT reported above. The treatment group experienced faster healing (mean days:  $10.2 \pm 0.9$  versus  $9.7 \pm 0.6$ ;  $p = 0.001$ ) Although the outcomes were statistically significant, the difference between the two regimens could not be considered clinically significant<sup>6</sup> (Level 1).

- In a comparative study<sup>12</sup> at high risk of bias, tilapia fish skin was applied to acute, non-infected full thickness limb burns ( $n = 4$ ) following surgical sharp debridement. The fish skin dressings were changed every five days. The outcomes were compared to those for burns on the contralateral limbs that received the local standard care (paraffin-impregnated gauze changed every three days). The mean Bates-Jensen Wound Assessment Tool (BWAT) scores on day 10 were not different (fish skin:  $18.75 \pm 1.25$  versus control:  $30.5 \pm 1.25$ ) (Level 2).
- An observational study ( $n = 18$ )<sup>13</sup> at high risk of bias, reported the effectiveness of shaour fish skin for treating partial-thickness burns. After preparation, the fish skin was applied to the burn area and secured with dry gauze. The fish skin dressing was replaced at day seven and day 15. The mean time to 90% epithelialisation was  $11.05 \pm 2.57$  days (range 7–15) and the mean time to 100% epithelialisation was  $17.27 \pm 2.05$  days (range 13–21). No cases experienced signs of local infection or allergic reaction<sup>13</sup> (Level 3).
- A case series<sup>4</sup> at high risk of bias reported the use of tilapia fish skin in split-skin graft donor sites for people ( $n = 10$ ) who had experienced burns. The fish skin was soaked in saline and applied directly to the donor sites, held in place with gauze. Dressings were changed on day 7 and then every three days. The average time to complete epithelialisation was 11.5 days (range 10–16) and the mean pain score on a VRS (0–10) at day 7 was 2.3 (range 1–4). In this study, an additional two participants received tilapia skin dressing applied to partial thickness burns, with complete epithelialisation observed at two weeks. No cases experienced signs of local infection (Level 4).
- Several case reports at high risk of bias describe the successful use of fish skin to treat partial thickness burns,<sup>1,2</sup> including burns in babies and young children.<sup>2</sup> In these case reports, healing occurred without complication in 10 to 17 days<sup>1,2</sup> (Level 4).

### Wound-related pain outcomes with fish skin dressing

Findings on the impact of tilapia fish skin dressing on wound-related pain are inconclusive. First, pain was only reported on unidimensional scales measuring pain intensity, and in many studies it was not clear when the pain assessment was conducted. When the results from three studies<sup>1, 6, 7</sup> were pooled in a meta-analysis,<sup>5</sup> tilapia fish dressing was associated with lower pain intensity but the result was not significant

(standard mean difference on a 10cm visual analogue scale (VAS)  $-0.608$ , 95% CI  $-0.885$  to  $-0.331$ ,  $p = 0.54$ ) (Level 1). The following results were reported in the primary research:

- Participants in the three-armed RCT<sup>7</sup> reported pain intensity using a 10cm VAS. There was no significant difference between pain intensity for tilapia fish skin dressing and silver sulphadiazine 1% cream in the arm in which participants had superficial second-degree burns to less than 10% of the body ( $p > 0.05$ ). In the arms in which participants had superficial second-degree burns to 10–20% of the body or deep second-degree burns to 5–15% of the body, those receiving tilapia fish skin dressing reported lower pain intensity immediately after dressing change than those receiving silver sulphadiazine 1% cream ( $p < 0.005$  for all wound dressing changes in both arms)<sup>7</sup> (Level 1).
- Participants in the second RCT<sup>6</sup> reported more rapid reduction in burn-related pain intensity ( $p < 0.001$ ) with a tilapia fish skin dressing compared to a control group receiving silver sulphadiazine 1% cream (Level 1).
- In the observational study ( $n = 18$ ),<sup>13</sup> the mean pain rating on a Verbal Rating Scale (VRS, 0–10) was  $6.94 \pm 0.72$  (range 6–8) at day 7, and this decreased statistically significantly ( $p < 0.001$ ) to  $5.22 \pm 0.64$  (range 4–6) at day 15 (Level 3).
- Individuals treated with fish skin dressing in other studies reported the dressing was comfortable.<sup>4, 12</sup>

### CONSIDERATIONS FOR USE

Consider local policies, procedures, and licensing before implementing traditional wound treatments.

#### Preparation

In the clinical studies,<sup>1, 2, 6</sup> the fish skin was sterilised using a chemical process followed by gamma irradiation and stored in sterile packaging under refrigeration prior to use. After preparation, the product can be stored in refrigerated sterile packaging for up to two years.<sup>2</sup>

#### Clinical use

- In clinical use,<sup>1, 6, 13</sup> burns were lightly debrided (if indicated) and then cleansed in sterile saline or a topical antimicrobial solution before fish skin was applied. The fish skin covered the entire wound or burn, including approximately 1cm of healthy peri-wound skin. The fish skin was covered with dry gauze with or without additional bandaging. In one study<sup>2</sup> the fish skin was washed in sterile 0.9% saline for 5 minutes three times immediately before its application to the burn.
- In most clinical reports, the fish skin dressing was checked every few days to ensure the fish skin adhered to the burn, but the fish skin was not replaced.<sup>1, 6, 7</sup> As the fish skin dries, it sloughs from the wound bed. At this stage, moistening the area (e.g., in the shower or using a cleansing solution) can assist in lifting the fish skin, revealing new epithelialisation.<sup>1</sup> In other reports, the fish skin dressing was replaced after 5 to 7 days.<sup>4, 12, 13</sup>

- Fish skin dressing may be inappropriate for some anatomical regions, including the face, neck and groin, due to difficulty achieving adequate adherence on skin folds.<sup>2,7,15</sup>

### Cost effectiveness

- Several sources<sup>1,7,12</sup> suggested that fish skin dressing is cost effective because the dressing does not need frequent replacement. In most reports in this evidence summary the fish skin was not replaced; in one study the fish skin dressing change was changed weekly<sup>13</sup> In the pooled results<sup>5</sup> from three studies<sup>1,6,7</sup>, tilapia skin dressing was associated with fewer dressings (SMD  $-4.195$ , 95% CI  $-5.615$  to  $-2.774$ ,  $p = 0.074$ ) but the result was not significant (*Level 1*).
- In an RCT<sup>6</sup>, there were significantly lower costs associated with using tilapia fish skin dressings compared with silver sulphadiazine cream ( $\$11 \pm \$1$  versus Brazilian  $\$19 \pm \$1$ ; dollars in 2020), related to lower costs for dressing materials and analgesia (*Level 1*).

### Adverse effects

Most of the research<sup>1,2,5-7</sup> included in this evidence summary reported no adverse events associated with fish skin dressings. In one small study<sup>12</sup>, two of the participants died due to septic shock deemed not related to either the fish skin dressing or the comparison paraffin-impregnated gauze dressing they were receiving.

### CONFLICTS OF INTEREST

The author declares no conflicts of interest in accordance with International Committee of Medical Journal Editors (ICMJE) standards.

### ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

WHAM evidence summaries are developed using methodology consistent with that published by Joanna Briggs Institute<sup>8-11</sup>. Evidence underpinning a WHAM recommendation is identified via a PICO search strategy, assigned a level of evidence and evaluated for risk of bias. All WHAM evidence summaries are peer-reviewed by an international Expert Reference Group. For more information on the methods and the WHAM Expert Reference Group, visit the website: [www.WHAMwounds.com](http://www.WHAMwounds.com).

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