Burns Open 9 (2025) 100385

Contents lists available at ScienceDirect

Burns Open

journal homepage: www.sciencedirect.com/journal/burns-open

Increasing experience in the use of papaya for burn injuries in an African context, potential and limitations

Helena W.C. Hofland [a,e], Edris W. Kalanzi [b], Emmie Viyuyi [c], Tilinde Chokotho [c], Titus M. Opegu [d], Eduard E. Zijlstra [e,*]

[a] Maasstadziekenhuis, Rotterdam, the Netherlands
[b] Burn and Plastic Surgery Department, Kiruddu Hospital, Kampala, Uganda
[c] Burn Unit, Queen Elizabeth Central Hospital, Blantyre, Malawi
[d] Midas Touch Medical Services, Kumi, Uganda
[e] Rotterdam Center for Tropical Medicine, Rotterdam, the Netherlands

ARTICLE INFO

Keywords:
Burn injuries
Treatment
Papaya
Africa

ABSTRACT

World-wide, burns are most common in low resource settings (LRS) with high mortality. Human resources, equipment and affordable, effective and safe treatments all influence outcome. Treatment of full thickness burns is particularly challenging and associated with high risk of complications. The presence of an eschar, infection and hypergranulation are important factors that delay wound closure. Tropical fruits are used for treatment of wounds and burns with excellent results. These fruits are usually available throughout the year and essentially inexpensive. The efficacy of papaya and pineapple is based on enzymes that have proteolytic activity and other compounds that have antimicrobial action. In the context of reverse technology, this enzymatic therapy has formed the basis of Nexobrid™ (based on enzymes derived from pineapple) that is now standard of care in high income countries. However, it is painful and very expensive. In LRS the use of papaya paste seems an alternative attractive option; however, evidence-based studies are needed on efficacy, safety, including standardization of the product used and treatment regimens.

1. Introduction

Burn injuries are among diseases associated with poverty [1]. Between 2009—2019 there were 9 million global burn cases and 111,000 deaths; 90 % of deaths occur in low- and middle-income countries (LMICs), 7 % in middle income countries and 3 % in high income countries (HIC) [2,3]. The risk of death is particularly high in children in LMICs [1]. Similarly, non-fatal burn injuries are an important cause of morbidity and disabilities; the global burden of Disability Adjusted Life Years (DALY) of 7.5 million DALY disproportionally affects LMICs in terms of welfare loss as share of Gross Domestic Product (GDP) [3].

In Africa, the cause of the poor outcome is multifactorial; burn injuries are part of many health challenges such malaria, tuberculosis and HIV/AIDS and in some settings, political instability plays a role [4]. However, delayed presentation is one of the commonest reasons for poor outcome in burn injuries in addition to shortage of doctors and nurses, and lack of equipment. Although burn centres have been established at the central level, people from rural areas often do not have access, because of cost and lack of transport. This causes delay in wound debridement and dressing which is paramount in burn care to relieve infection, which is essential for burn healing [4,5] (https://www.afro.who.int/health-topics/traditional-medicine). The ISBI Guidelines aimed to create Practice Guidelines for burn care to improve the care in both Low Resource Settings (LRS) and resource-abundant settings [6,7]. If in deep partial thickness and full thickness wounds early excision and skin grafting are not possible, the open technique (exposure) may be applied until eschar separation has begun [6,7]. This means that after 4–5 days the wound may be infected with active invasion of unburned surrounding tissues with risk of sepsis and death. Keeping the wound dry may help in controlling bacterial infection for wound closure and separation of the eschar; the latter is essential as below the eschar infection continues and there is no exposure to immune responses. The closed technique includes application of topical antimicrobial agents such as silver sulphadiazine (SSD), silver nitrate solution or silver releasing dressings (relatively expensive); cerium nitrate (relatively inexpensive) and antiseptic solutions such as Dakin's solution, acetic acid

* Corresponding author at: Bovenstraat 21, Rotterdam Center for Tropical Medicine, The Netherlands.
E-mail address: e.e.zijlstra@roctm.com (E.E. Zijlstra).

https://doi.org/10.1016/j.burnso.2024.100385
Received 17 September 2024; Received in revised form 18 November 2024; Accepted 25 November 2024
Available online 27 November 2024

Table 1
Studies on the use of papaya in (full thickness burn) wounds in low-resource settings.

Country	Study design	Type of wound	Patients	Regimen used	Outcome	Side-effects	Reference
Pakistan	Case series	Deep burns (TBSA 10–35 %)	N = 30	Papaya daily dressings, 5–7 total	Healing in 27, minor surgical debridement in 3	Well tolerated	(25)
India	Case series	Second- and third-degree burns (TBSA 10–60 %)	N = 50	Papaya daily dressings for a week	Eschar became loose in all, could be removed by surgical debridement	Slight burning pain; no withdrawal from study	(26)
The Gambia	Case series	Paediatric burns, full thickness and infected burns	N = 32	Mashed papaya pulp spread on gauze applied daily	Wounds become clean for grafting	Well tolerated	(13)
Nigeria	Prospective, comparative	Wound: 45 % traumatic, 24 % infective	N = 32 unripe papaya dressing N = 32 honey dressings	Grated unripe papaya, or laser honey (radiated for sterility), alternate day dressings	Papaya: mean eschar separation time 5.5 days vs honey 30 days; bacterial clearance for papaya 6.8 vs 15.3 days for honey	Not reported	(27)
Nigeria	Case series	Wounds requiring debridement	N = 30	Unripe papaya	Eschar separation mean 5.5 days (SD 2.26) bacterial clearance mean 6.7 days (SD 3.75)	No side-effects	(28)
Jamaica	Self-administered questionnaire among ~ 200 nurses	Chronic ulcers	Unknown	Unripe papaya	More effective than other applications	Occasionally burning sensation	(16)

(inexpensive, availability varies) or 0.006 % unbuffered sodium hypochlorite solution (inexpensive, widely available) [6,7]. Slow separation of the eschar is a disadvantage.

1.1. *Alternative treatment*

Given these restrictions in availability and cost, and the high morbidity and mortality, burn centers in LRS have looked for alternative treatment that are effective, safe, cheap and locally available, particularly traditional burn care [8–10].

A moist wound environment may be promoted by lubricating jelly. For example, petroleum jelly gauzes are used as emollients and are made locally; alternatively banana leaves or boiled potato peel may be used [8].

For debridement and treating infected wounds, phytotherapy may be considered [6–8]. This encompasses the use of herbal agents (plant parts or materials) as well as excipients (solvents, diluents or preservative) and is popular among 4 billion people in the absence of affordable or available drugs and because they are perceived as safe. They are mostly used in treatment of wounds. Phytotherapeutic agents are standardized herbal preparations and include, among other, aloe vera, tea tree oil, jojoba, garlic, ginseng olive oil, rosemary and papaya [11]. While the market of phytotherapeutic agents is increasingly regulated, data on quality, safety and efficacy are often not available [12].

Tropical fruits such as papaya are available the whole year and are very cheap; it contains enzymes of which papain seems most active; it is a protease and is used as a meat tenderizer; other enzymes include leucopapain that seems to have an effect as a de-sloughing agent, and chymopapain. Other components include carpaine and aglycones that have broad spectrum antibiotic activity [13].

While papaya and papain have been studied as a promising form of enzymatic debridement since the 1940s, to date the scientific basis for their use is limited [14].

Papaya (*Papaya carica,* "the melon tree") is also known as paw-paw, and as "common man's fruit" because of its low cost and high nutritional value [15]. Treatment usually takes the form of pulp from the green (unripe) papaya that is rich in papain and has been widely used in the treatment of skin ulcers by traditional healers [16–18]. The fruit is washed, peeled, seeded and mashed into a paste and applied undiluted on the wound. One large papaya can be used for more than one patient and can be stored for at least 24 h [9,13,16].

Animal studies showed a beneficial effect of papaya in excision wounds in diabetic rats by induction of granulation tissue. This may be induced by increased levels of hydroxyproline; vitamin C, abundantly present in papaya converts proline to hydroxyproline that is an indicator of collagen deposition. The wound-debriding effects are attributed to enzymes such as papain and chymopapain [13].

In addition papaya has an antibacterial effect on common microorganisms causing infection that include gram-positive and gram- negative organisms; in papaya seeds, inhibition was strongest in *B cereus* > *E coli* > *S faecalis* > *S aureus* > *P vulgaris* > *S flexneri* and independent on the stage of fruit maturity (immature, mature or ripe fruits); there was no effect of epicarp or endocarp extracts [13,19–21], In addition, there is an indirect effect on infection as the enzymes remove the necrotic debris, thus breaking down the biofilm (crust) leading to exposure to ultraviolet light and host immune responses [22]. Animal studies also showed induction of granulation tissue [19].

Human studies have been done in patients with burns or chronic nonhealing ulcers such as caused by pressure, diabetes mellitus or venous ulcers [16]. Recently, a systemic review and *meta*-analysis was published on the use of *Carica papaya* in wound healing in diabetic foot ulcer; in 5 randomized controlled trials papaya had a good effect on wound healing and reduced necrosis [23]. In another study, papaya was used successfully in incision wounds in post-caesarean section patients with wound dehiscence (gape) [22,24].

Papain (EC: 3.4.22.2) may be used for external conditions (jellyfish

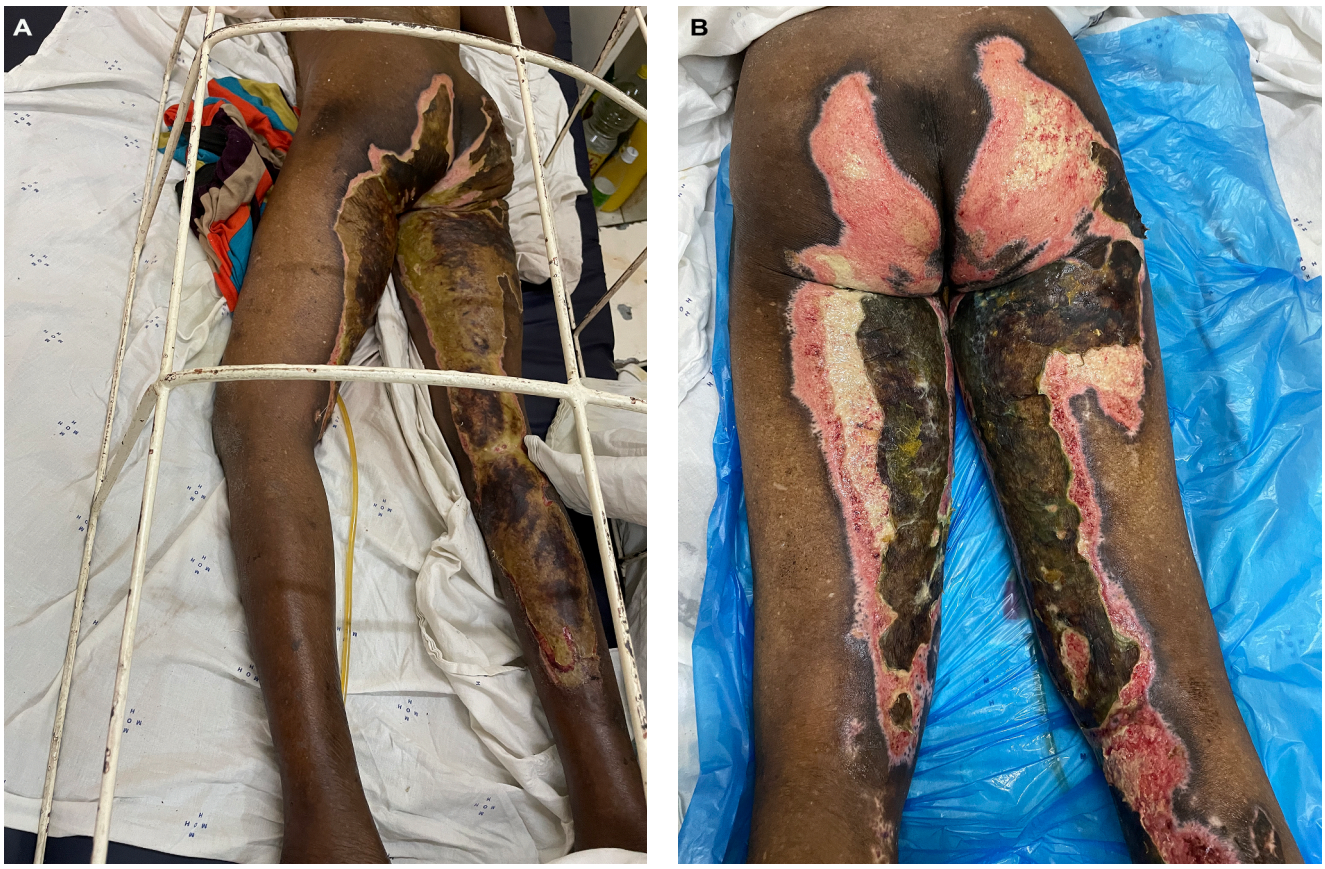

Fig. 1. A. Despite treatment for two weeks with EUSOL/paraffine, the necrosis remained unchanged. B. After 4 days, the necrosis on her buttocks and calf on the right leg was easily removed. Granulation tissue was noted, and the wound healed progressively.

stings, shingles, wound healing) and internal conditions (dental cavities, parasite infections, digestive problems [bloating, oesophageal reflux, constipation]) and many other conditions, but there is no good scientific evidence to support these applications.

Papain is a purified protein extracted from the latex of the unripe papaya; it is a protease and may be used instead of papaya as a phytotherapeutic agent to debride wounds, lesions, ulcers, and burned skin without causing adverse effects [29]. Papain was demonstrated to be a powerful antioxidant against H_2O_2 induced damage and was found not to be toxic or mutagenic [30]. It is available as a commercially prepared powder used for GI problems and as a meat tenderizer [9]. In Brazil, it is mixed with a gel, sterile water or normal saline by nurses in hospital; concentrations may vary from 1-4 % for slough or granulated tissue to 10 % for black necrosis. For use at home, a 4 % solution papain gel may be used, obtained from the pharmacy. No prescription is needed. More than 5,000 patients were successfully treated [9]. The use of papain in active pharmaceutical ingredient (API) in dressings make it easier to apply and remove, providing greater comfort to the patient and prolonged drug action [30]. However, free papain can undergo deactivation when exposed to adverse environmental conditions. To solve this problem, the immobilization of the enzyme on a polymeric support is used [11]. It is sometimes in association with hydrous magnesium silicate (talc powder) or alginate [31,32].

Debridace™ was a promising papain urea compound but proved to be disappointing as it produced high fever and /or excruciating pain in 30 consecutive major burn patients with only 2 patients who completed the study [33]. Other than papaya, papain may cause an immediate hypersensitivity reaction by direct contact when applied on a wound, or by inhalation causing acute rhino-conjunctivitis, bronchitis or an asthmatic attack, mainly during occupational exposure, or by ingestion when papain has been used as a meat tenderizer [34–38].

2. Use in Africa

While most practical experience has been gained in poor Asian areas, there are few reports from Africa [25–28]. Studies in burn patients with papaya from LRS are summarized in Table 1; there is only 1 study from Africa (the Gambia) that solely focused on burns. All showed good efficacy; the eschar became loose and could be removed by simple surgical debridement; pink and healthy granulation tissue followed. Early debridement, less surgical interventions, less anaesthesia time, less blood transfusions and healthy granulation tissue were considered major benefits [39]. Side-effects were mild and there was no evidence of hypersensitivity reactions in the use of papaya [13,16]. Although partial thickness wounds should primarily be treated with petroleum jelly gauze, one study reported conversion into a full thickness wound, possibly due to papaya [13].

We report increased clinical experience with papaya in 4 patients from Malawi, Mozambique and Uganda, each with a specific indication.

Fig. 2. A. The mixed thickness burn was treated with honey. Hypergranulation developed. B. Papaya treatment was started. After 4 days the hypergranulation tissue had considerably reduced.

2.1. Case reports

1. Full thickness burn at Queen Elizabeth central Hospital, burn Unit, Blantyre, Malawi

An 80-year-old woman warmed herself near open fire. Her *chitenje* (traditional African wrapper) which covered her dress caught fire. No first aid was given apart from removal of her burning clothes. She sustained a full thickness burn. TBSA was 12 % located on the buttocks, and at the dorsal side of both legs. Due to her age and the lack of blood transfusions, the decision was made to treat the wound conservatively. For two weeks treatment was with EUSOL (Edinburgh University Solution of Lime)/paraffine, the necrosis remained unchanged. Then the treatment changed to papaya mash. After 2 days of treatment of papaya the necrotic tissue became softer. After 4 days, the necrotic tissue on her buttocks, calf on right leg was easily removed. Granulation tissue was seen, and some areas progressively healed. When only 4 % of TBSA on the leg and the calf remained, surgical debridement and grafting was done. She went home completely healed. (Fig. 1).

2. A mixed thickness burn in rural Mozambique

In a rural area a young girl sustained a mixed thickness burn. She was treated by local volunteers in the area. Because of lack of progress, Dutch burn professionals were asked for advice, but topical agents were not available and referral to a local hospital for skin grafting was not possible because of major logistic problems. Then she was treated with honey which speeded up the healing, until hypergranulation appeared. Again, advice was sought, and papaya treatment was started instead. Only 4 days later the hypergranulation had considerably reduced with progressive healing. (Fig. 2).

3. A mixed thickness burn in Kiruddu Hospital, Kampala, Uganda

A young girl was admitted with a mixed thickness burn on her legs and abdomen, reportedly because of hot water. First aid measures were not taken. Management with povidone iodine every three days resulted in healing. However, thick necrotic tissue remained and did not subside. Papaya treatment started and the thick necrosis loosened and could be removed after 2 treatments of papaya. The remaining skin defect was treated with a honey dressing, and she was discharged and followed-up in the out-patient department to monitor if grafting in the future was necessary. (Fig. 3).

4. Full thickness burn in Kiruddu Hospital, Kampala, Uganda

A 38-year-old man sustained burns on his face, chest, both arms because of an explosion. After admission he was resuscitated and after that surgical debridement was performed and wound management with a silver dressing started. Unfortunately, the non-viable tissue was not completely removed. In a discussion with the patient papaya treatment was mentioned. It appeared his first choice and his wife bought papaya and mashed it so the nurses could use it without further preparation.

After three days, both the patient and his wife were very happy and sent the author these pictures. Healthy granulation tissue was visible, and patient was booked for grafting as soon as possible. (Fig. 4).

2.2. Clinical experience with papaya

2.2.1. Application

There is no standardization on the selection of papaya (unripe or [partially] ripe), preparation of the dressing (mashed or extract) and method of application [22]. It is not clear whether the papain content and antibacterial activity varies in the different stages of ripening and whether this has an effect on efficacy [9].

Ripe papaya is easiest to apply and comfortable for the patient; after discarding the seeds and the skin, the paste is put on a dry gauze and fixed with bandage. (Fig. 5) One papaya can be used for several patients, depending on the surface of the burned area. The papaya can be stored in the fridge for 3 days. Dressings may be changed daily or every other day. The duration of treatment depends on the indication; for loosening of the eschar 2 – 3 new dressings every other day, for hypergranulation or infection / dirty wounds 1 – 2 dressings are usually sufficient [13,24,40].

2.2.2. Acceptance and tolerability

Currently, there is no patient information on the expected outcome or side-effects and the management thereof [8]. Patients and nurses need to be convinced because they eat papaya and cannot believe it will do any good to their wounds. This is invariably overcome once seeing the result. (HWC Hofland, personal communication). Papaya fruit is cheap and readily available.

Papaya treatment is not painful. Sometimes mild itching is reported. No allergic reactions have been demonstrated. Dressing using ripe papaya is comfortable unlike unripe papaya that needs to be grated, the bandage feels more solid and is more problematic in fixation, therefor overall less comfortable for the patient. (HWC Hofland, personal communication).

Fig. 3. A. Healed burn with thick necrosis; papaya treatment was started. B. After 2 days necrotic tissue became loose; after 4 days the eschar could be removed.

3. Discussion

The use of tropical fruits such as papaya has formed the basis of enzymatic debridement in burn care in high income countries as an example of reverse technology. NexoBrid ™ (bromelain-based anacaulase-bcdb) is a topically administered, bromelain-based biological product from the pineapple plant (*Ananas comosus*) containing a sterile mixture of proteolytic enzymes. The product selectively removes burn eschar within 4–6 h without harming surrounding viable tissue. The application is extremely painful and needs to be applied and removed under block or general anaesthesia, or in the ICU under general sedation using continuous intravenous administration of opioids. Its effect has been studied in various trials and this treatment modality is now integrated in European Guidelines [41,42]. It is expensive; a 5 g package (cost per unit 839.27 euros), can be applied to approximately 2.5 % of TBSA [43]. However, randomized studies have shown a decrease of the need of surgical debridement, more rapid complete eschar removal, and lower percentage of autograft surgery and blood loss, resulting in considerable reduction of overall cost [43].

Clearly, the complex clinical management, the need for strong opioid pain medication, anaesthetic requirements and cost are unrealistic challenges for LRS, leaving an urgent need of effective and affordable treatments in full thickness wounds. In clinical practice, it is often not possible to apply the standards as outlined by the ISBI Practice Guidelines. The use of tropical fruits such as papaya and other locally available products is attractive and increasingly used as phytotherapy in burns and other wounds. Papaya is preferred as it is available the whole year through and very cheap, while pineapple is seasonal and marginally more expensive.

While there are no research data comparing the efficacy and safety with other, more conventional, treatment modalities, the use of papaya seems justified in alleviating patients suffering and reducing the risk of long-term complications; no serious side-effects have been reported and these readily available treatments are of low cost.

There is no doubt that there is a need for research in terms of standardization, side-effects, dose and duration of treatment, antibacterial properties, mode of administration, need to autoclave, and storage, among other things. Mutagenicity, hypersensitivity and systemic absorption need to be explored. Without these data, it is impossible to inform patients on outcome or side-effects. Once these data are obtained, these products ideally would be available after Good Manufacturing Practice (GMP) and tested in randomized controlled trials according to Good Clinical Practice (GCP) to obtain evidenced-based data. Obviously, it will take time, commitment and funding to develop these products that most likely may be costly initially. Until then, given the poor outcome of full thickness burns in LRS, the benefits of locally and widely accepted treatment using tropical fruits such as papaya seem to outweigh the concerns listed and in absence of alternative treatments, the use of these products seems justified on a case-by-case basis. Standardized reporting and monitoring will be important.

Fig. 4. A. The necrotic tissue was removed surgically, leaving an infected wound after 6 days. B. Nurse applies papaya gauzes. C. After 3 days the wound had improved and was ready for grafting.

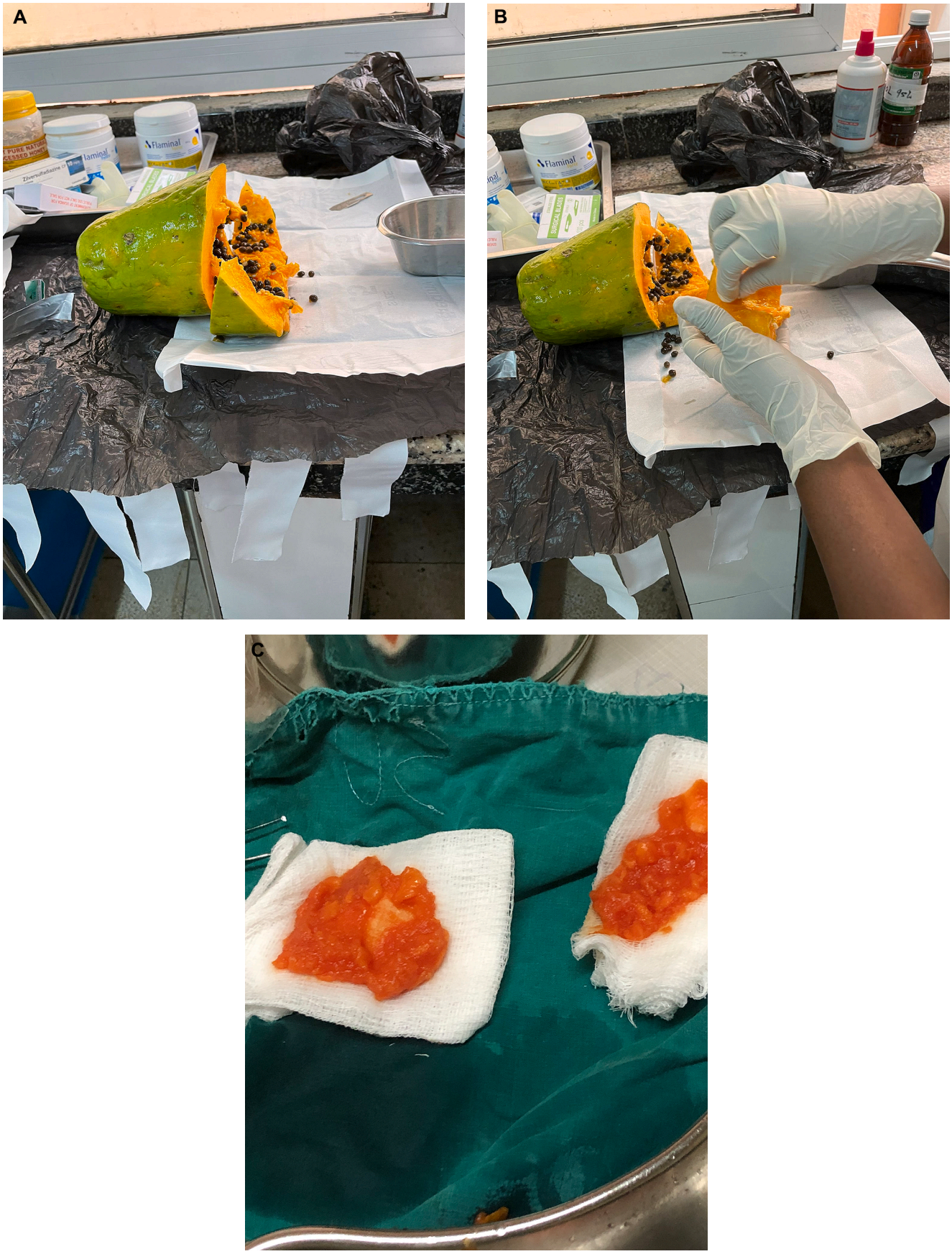

Fig. 5. A. Cutting the papaya. B. Removing the seeds and mash the papaya. C. Ready for use on a patient. Papaya mash on a dry gauze.

4. Patient consent

Informed consent was obtained from all patients.

Ethical approval

Not required.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Helena W.C. Hofland: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Edris W. Kalanzi:** Investigation, Writing – review & editing. **Emmie Viyuyi:** Investigation, Writing – review & editing. **Tilinde Chokotho:** Investigation, Writing – review & editing. **Titus M. Opegu:** Investigation, Writing – review & editing. **Eduard E. Zijlstra:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

We are most grateful to Professor H.J. Klasen for critically reading the manuscript.

References

[1] Peck MD. Epidemiology of burns throughout the world. Part I: distribution and risk factors. Burns 2011;37(7):1087–100.
[2] Mashreky SR, Rahman A, Chowdhury SM, Giashuddin S, Svanstrom L, Khan TF, et al. Burn injury: economic and social impact on a family. Public Health 2008;122 (12):1418–24.
[3] Gerstl JVE, Ehsan AN, Lassaren P, Yearley A, Raykar NP, Anderson GA, et al. The global macroeconomic burden of burn injuries. Plast Reconstr Surg 2024;153(3): 743–52.
[4] Lindert J, Bbaale D, Mohr C, Chamania S, Bandyopadhyay S, Boettcher J, et al. State of burns management in Africa: challenges and solutions. Burns 2023;49(5): 1028–38.
[5] Stevenson JH, Borgstein E, Broadis E, Chokotho T, Watson S. Global surgery and burn injuries; experience from a 25 year partnership in Malawi. Surgeon 2021;19 (6):338–43.
[6] ISBI Practice Guidelines for Burn Care, Part 2. Burns. 2018;44(7):1617-706.
[7] ISBI Practice Guidelines for Burn Care. Burns. 2016;42(5):953-1021.
[8] Benskin LL. A review of the literature informing affordable, available wound management choices for rural areas of tropical developing countries. Ostomy Wound Manage 2013;59(10):20–41.
[9] Pieper B, Caliri MH. Nontraditional wound care: a review of the evidence for the use of sugar, papaya/papain, and fatty acids. J Wound Ostomy Continence Nurs 2003;30(4):175–83.
[10] Albertyn R, Berg A, Numanoglu A, Rode H. Traditional burn care in sub-Saharan Africa: a long history with wide acceptance. Burns 2015;41(2):203–11.
[11] Pazyar N, Yaghoobi R, Rafiee E, Mehrabian A, Feily A. Skin wound healing and phytomedicine: a review. Skin Pharmacol Physiol 2014;27(6):303–10.
[12] Calixto JB. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). Braz J Med Biol Res 2000;33(2): 179–89.
[13] Starley IF, Mohammed P, Schneider G, Bickler SW. The treatment of paediatric burns using topical papaya. Burns 1999;25(7):636–9.
[14] Klasen HJ. History of Burns. Rotterdam, The Netherlands: Erasmus Publishing; 2004.
[15] Koul BP, Sharma C, Kumar A, Sharma V, Yadav D, Jin J. Carica papaya L.: a tropical fruit with benefits beyond the tropics. Diversity 2022;14:683.
[16] Hewitt H, Whittle S, Lopez S, Bailey E, Weaver S. Topical use of papaya in chronic skin ulcer therapy in Jamaica. West Indian Med J 2000;49(1):32–3.
[17] Vijayakumar S, Morvin Yabesh JE, Prabhu S, Manikandan R, Muralidharan B. Quantitative ethnomedicinal study of plants used in the Nelliyampathy hills of Kerala. India J Ethnopharmacol 2015;161:238–54.
[18] Yabesh JE, Prabhu S, Vijayakumar S. An ethnobotanical study of medicinal plants used by traditional healers in silent valley of Kerala. India J Ethnopharmacol 2014; 154(3):774–89.
[19] Nayak BS, Ramdeen R, Adogwa A, Ramsubhag A, Marshall JR. Wound-healing potential of an ethanol extract of Carica papaya (Caricaceae) seeds. Int Wound J 2012;9(6):650–5.
[20] Dawkins G, Hewitt H, Wint Y, Obiefuna PC, Wint B. Antibacterial effects of Carica papaya fruit on common wound organisms. West Indian Med J 2003;52(4):290–2.
[21] Emeruwa AC. Antibacterial substance from Carica papaya fruit extract. J Nat Prod 1982;45(2):123–7.
[22] Murthy MB, Murthy BK, Bhave S. Comparison of safety and efficacy of papaya dressing with hydrogen peroxide solution on wound bed preparation in patients with wound gape. Indian J Pharmacol 2012;44(6):784–7.
[23] Siva SS, Prakash S, Titus J, Fazulah MAM, Suriyakala V. Effectiveness of conventional management and Carica papaya on influencing wound healing: a systemic review and meta-analysis. Biomedicine 2023;43(3):825–30.
[24] Nisa MS. Enzymatic wound debridement; role of papaya in the management of post cesarean gaped wounds. Annals 2012;18:355–9.
[25] Rashid SK, Iqbal Y. Role of topical papaya application in debridement of deep burn wounds. Journal of Rawalpindi Medical College 2021;25(2):171–4.
[26] Jayarajan RCN, Adenwalla HS. Papaya pulp for enzymatic wound debridement in burns. Indian Journal of. Burns 2016;24:24–8.
[27] Nnadozie UU, Maduba CC, Modekwe VI, Obayi NOK, Amu OC, Onyebum OV, et al. Wound bed preparation using nonsurgical methods: a prospective comparative study of honey versus unripe papaya (Carica papaya). Ann Afr Med 2023;22(4): 515–9.
[28] Maduba CC, Nnadozie UU, Modekwe VI, Maduba V, Okorie GM, Onyebum VO. Wound bed preparation using unripe pawpaw in a resource-poor environment: a prospective study. World J Plast Surg 2022;11(1):59–63.
[29] Ajlia SA, Majid FA, Suvik A, Effendy MA, Nouri HS. Efficacy of papain-based wound cleanser in promoting wound regeneration. Pak J Biol Sci 2010;13(12): 596–603.
[30] da Silva CR, Oliveira MB, Motta ES, de Almeida GS, Varanda LL, de Padula M, et al. Genotoxic and cytotoxic safety evaluation of papain (Carica papaya L.) using in vitro assays. J Biomed Biotechnol 2010;2010:197898.
[31] Moreira Filho RNF, Vasconcelos NF, Andrade FK, Rosa MF, Vieira RS. Papain immobilized on alginate membrane for wound dressing application. Colloids Surf B Biointerfaces 2020;194:111222.
[32] da Silva Melo AEC, de Sousa FSR, Dos Santos-Silva AM, do Nascimento EG, Fernandes-Pedrosa MF, de Medeiros C, da Silva-Junior AA. Immobilization of papain in chitosan membranes as a potential alternative for skin wounds. Pharmaceutics 2023;15(12).
[33] Langer V, Bhandari PS, Rajagopalan S, Mukherjee MK. Enzymatic debridement of large burn wounds with papain-urea: Is it safe? Med J Armed Forces India 2013;69 (2):144–50.
[34] Soto-Mera MT, Lopez-Rico MR, Filgueira JF, Villamil E, Cidras R. Occupational allergy to papain. Allergy 2000;55(10):983–4.
[35] Quarre JP, Lecomte J, Lauwers D, Gilbert P, Thiriaux J. Allergy to latex and papain. J Allergy Clin Immunol 1995;95(4):922.
[36] Novey HS, Keenan WJ, Fairshter RD, Wells ID, Wilson AF, Culver BD. Pulmonary disease in workers exposed to papain: clinico-physiological and immunological studies. Clin Allergy 1980;10(6):721–31.
[37] Mansfield LE, Bowers CH. Systemic reaction to papain in a nonoccupational setting. J Allergy Clin Immunol 1983;71(4):371–4.
[38] Yokozeki K, Yuki T, Ogasawara A, Katagiri A, Takahashi Y, Basketter D, et al. Total dose defines the incidence of percutaneous IgE/IgG1 mediated immediate-type hypersensitivity caused by papain. J Appl Toxicol 2021;41(6):898–906.
[39] Jayarajan RCN, Adenwalla HS. Papaya pulp for enzymatic wound debridement in burns. Indian J Burns 2016;24:24–8.
[40] Atiyeh B, Makkawi K, Beaineh P. Burn Wounds And Enzymatic Debridement (Ed) - Past, Present, And Future. J Burn Care Res 2024;45(4):864–76.
[41] Hirche C, Kreken Almeland S, Dheansa B, Fuchs P, Governa M, Hoeksema H, et al. Eschar removal by bromelain based enzymatic debridement (Nexobrid(R)) in burns: European consensus guidelines update. Burns 2020;46(4):782–96.
[42] Rosenberg L, Shoham Y, Krieger Y, Rubin G, Sander F, Koller J, et al. Minimally invasive burn care: a review of seven clinical studies of rapid and selective debridement using a bromelain-based debriding enzyme (Nexobrid(R)). Ann Burns Fire Disasters 2015;28(4):264–74.
[43] Giudice G, Filoni A, Maggio G, Bonamonte D, Vestita M. Cost analysis of a novel enzymatic debriding agent for management of burn wounds. Biomed Res Int 2017; 2017:9567498.