Acta Manilana 73 (2025), 113-128

ISSN: 0065-1370

Acta Manilana

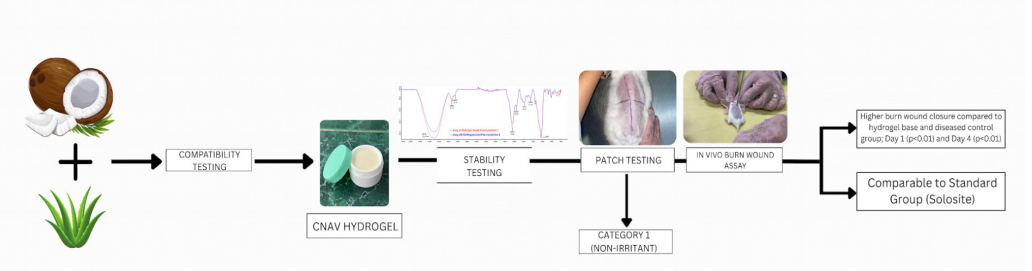
journal homepage: https://actamanilana.ust.edu.ph/

Formulation and Evaluation of *Cocos nucifera-Aloe vera* Hydrogel for Burn Wound Healing

Zach Devashka A. Masangkay[1], Mikaela Rosalen R. Mercado[1], Julia Tashana D. Navarrete[1], Adrian Joash S. Pamani[1], Katrina S. Ramos[1], Dannah Alezandra E. Reyes[1], Ana Marie L. Rubenicia[1], and Agnes L. Llamasares-Castillo[1,2,3]*

[1]Department of Pharmacy, Faculty of Pharmacy, University of Santo Tomas
[2]Graduate School, University of Santo Tomas
[3]Research Center for the Natural and Applied Sciences, University of Santo Tomas

Graphical Abstract



Abstract

Burn injuries remain a major global health concern, particularly in low-resource areas with limited access to effective care. This study aimed to develop a cost-effective natural hydrogel for burn treatment using *Cocos nucifera* endosperm and *Aloe vera* (CNAV), both of which are known for their wound-healing properties. Excipient compatibility was evaluated using Fourier-Transform Infrared (FTIR) spectroscopy and organoleptic assessment. Three hydrogel formulations were prepared and tested for stability and compatibility. Safety was evaluated through a patch test on albino rabbits, while efficacy was assessed in vivo using BALB/c mice with full-thickness burns. Test animals were divided into four groups: diseased control, negative control (hydrogel base), standard (Solosite Wound Gel), and experimental (CNAV hydrogel). Wound healing progress was monitored through closure rate and visual observation. The CNAV hydrogel was classified as a non-irritant (Category 1) based on the 2019 UN GHS criteria. It showed significantly faster wound closure on Days 1 and 4 ($p<0.01$) compared to control groups, performing comparably to the commercial standard. In conclusion, the CNAV hydrogel is stable, safe, and effective in promoting burn wound healing, supporting its potential as a natural, affordable, and accessible alternative to conventional treatments

Keywords: *Cocos nucifera*; *Aloe vera*; hydrogel formulation; wound healing

Corresponding author: alcastillo@ust.edu.ph
DOI: https://doi.org/10.53603/actamanil.73.2025.mnvr5392

Date Received: 10 November 2025
Date Revised: 09 December 2025
Date Accepted: 09 December 2025

Introduction

Burns are the world's fourth most frequent type of injury, after motor vehicle accidents, falls, and physical violence [1,2]. They cause approximately 180,000 deaths annually, with the highest burden seen in low- and middle-income countries, particularly in Africa and Southeast Asia. In the Philippines, the Philippine General Hospital Alfredo T. Ramirez Burn Center (PGH-ATR) reported 2,492 admissions between 2013 and 2019, highlighting the persistent burden of burn injuries in the region [3].

Hydrogels have emerged as a valuable therapeutic option for burn wounds due to their ability to maintain a moist healing environment, promote gas exchange, and absorb wound exudate [1, 2]. Their softness, malleability, and biocompatibility make them suitable for damaged skin, while the incorporation of antimicrobial or anti-inflammatory agents further enhances their clinical utility [4,5].

Cocos nucifera (L.) and *Aloe vera* are two natural products widely recognized for their wound-relevant properties. *C. nucifera*, particularly in the form of hydrolyzed virgin coconut oil, exhibits anti-inflammatory and antimicrobial effects and has demonstrated concentration-dependent improvement in burn wound healing, with higher hydrolyzed formulations promoting faster recovery [6]. *Aloe vera*, similarly, is known for its strong anti-inflammatory activity, antioxidant effects, and ability to maintain moist wound conditions that support the migration of fibroblasts and epidermal cells, resulting in improved wound closure in experimental models [7, 8]. Given the continuing burden of burn injuries and the need for accessible, cost-effective interventions, combining the complementary wound-healing properties of *C. nucifera* and *Aloe vera* into a hydrogel system presents a promising therapeutic approach. Such a formulation may enhance healing outcomes and offer an affordable option for patients in resource-limited regions.

Materials and Methods

Materials. All excipients used in the three test hydrogel formulations were of analytical grade. Tiletamine-zolazepam was used to place the BALB/c mice under anesthesia during the burn induction. Solosite Wound Gel (Smith & Nephew) was used as a standard for comparison with the formulated hydrogel.

Plant sample collection and preparation. The plants, coconut (*Cocos nucifera*) and *Aloe vera*, were obtained from San Andres Street, Malate, Manila, Philippines, and North Susana Avenue, Quezon City, Philippines, respectively, and identified at the UST RCNAS Herbarium. The endosperm from the coconut fruit was cut with a knife and rinsed with distilled water [9]. The gel from the *Aloe vera* leaves was extracted, washed with mild chlorine solution, and rinsed with distilled water [10]. Both plant materials were homogenized using a blender [9, 10].

Characterization. The coconut endosperm and *Aloe vera* gel were subjected to characterization. The results for each plant were compared to the official monographs for organoleptic characterization [11, 12], pH [13, 14], specific gravity [15, 16], and viscosity [17].

Lyophilization. The homogenized coconut endosperm and *Aloe vera* gel were lyophilized using a Zirbus VaCo 5 Freeze-Dryer for 96 hours, which afforded a %yield of 11.52% and 3.86%, respectively.

FTIR Analysis. Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (FTIR-ATR) Bruker/Alpha II was used to evaluate the compatibility between the active pharmaceutical ingredients (API) and various excipients [18]. Individual spectra were first obtained from each excipient and the active ingredients. A mixture of lyophilized *C. nucifera* endosperm and lyophilized *Aloe vera* gel was prepared and combined separately with each pharmaceutical excipient. Each combination was subjected to FTIR-ATR. Spectral comparisons were done to detect significant changes, which may indicate potential incompatibility.

Hydrogel Formulation. Three hydrogel formulations were developed using compatible excipients, each containing 10 grams of lyophilized *C. nucifera* endosperm and lyophilized *Aloe vera* (CNAV) gel. All three formulations were compounded using simple dissolution and incorporation without the aid of heat.

The first formulation consisted of HPMC, Carbopol, glycerin, potassium sorbate, sodium benzoate, acacia gum, ascorbic acid, tartaric acid, and distilled water [19].

The second formulation consisted of sodium alginate, glycerol (86%), calcium chloride (0.5%), DMSO, and distilled water [20].

The third formulation was compounded with methylcellulose that was hydrated overnight in distilled water, mixed with propylene glycol, methylparaben, triethanolamine, and distilled water [21].

Quality Control. The pH, spreadability, homogeneity, viscosity, chemical stability, and storage stability were assessed at Days 0 and 29 of the hydrogel's storage. The pH was determined with a pH meter calibrated using two standard buffers at pH 4 and pH 7 [22]. For spreadability, 1 g of the hydrogel was compressed between two glass slides using a 100 g weight for 60 seconds. The spread's diameter was measured and used to compute the spreadability [23]. For homogeneity, the CNAV hydrogel was visually inspected to confirm a homogenous appearance. Viscosity was measured using a Brookfield viscometer with an RV-03 spindle at 10 rpm [24]. FTIR-ATR (Bruker/Alpha II) was used to evaluate the stability of the formulated CNAV gel by comparing the spectra at Days 0 and 29 of storage [25].

In vivo studies. Both Acute Dermal Irritation Patch Test and Assay for wound healing property using full-thickness burns in Balb/c mice were conducted according to the protocol and guidelines approved by the Institutional Animal Care and Use Committee (IACUC) of University of Santo Tomas (RC2024-451213 approved on February 3, 2025).

Acute Dermal Irritation Patch Test. The procedure was based on the OECD Guideline 404 for acute dermal irritation. Four female albino rabbits were used, and the dorsal areas were shaved 24 hours before the test and divided into four quadrants (approx. 6 cm^2 each).

The formulated CNAV hydrogel (0.5g) was applied to Quadrants 1 and 4, while the hydrogel base (0.5g) was applied to Quadrant 3, and Quadrant 2 was left untreated. The treatments were held in place with gauze and medical tape for 4 hours. Afterward, the patches were removed, and the skin was rinsed with distilled water. Using the OECD scoring system (Table 1), erythema and edema were scored blindly at 1, 24, 48, and 72 hours after the patches were removed. The scores were used to calculate the Primary Irritation Index (PII) as shown in Figure 1. The PII was then classified using the UN GHS 2019 classification for skin irritancy of test chemicals [9, 26].

Burn Induction. This study employed a modified murine thermal burn model to induce full-thickness burns [22]. Twenty healthy female BALB/c mice were randomly divided into four experimental groups, each consisting of five mice: a diseased control group (no treatment), a standard group (Solosite), a negative control group (hydrogel base), and an experimental group (CNAV hydrogel). The mice were placed under anesthesia using tiletamine-zolazepam through the intraperitoneal route by a licensed veterinarian. The dorsal side of each mouse was shaved and marked with 11 x 6 mm areas, and was disinfected with 70% ethanol. In each mouse, the circular end of a nichrome rod (6 mm diameter) was heated over an open flame to 150°C. The heated rod was pressed onto the marked 11 mm × 6 mm area two times, with each contact lasting 5 seconds, to ensure complete coverage and uniform burn induction across the entire area [27].

Treatment. After the burn induction, the BALB/c mice were treated immediately and accordingly, with a regimen that continued for a 14-day period. About 100 mg of the assigned treatment was applied topically on the affected area of each mouse every morning.

Table 1. OECD Guideline 404 Scoring System for Edema and Erythema Formation [10].

Edema Formation	No edema	0
	Very slight edema	1
	Slight edema (edges of area well defined by definite rating)	2
	Moderate edema (raised approximately 1 mm)	3
	Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4
Erythema Formation	No erythema	0
	Very slight erythema (barely perceptible)	1
	Well-defined erythema	2
	Moderate to severe erythema	3
	Severe erythema (beef redness) to eschar formation, preventing grading of erythema	4

$$PII = \frac{\sum(Erythema)+\sum(Edema) \ at\ 1, 24, 48, and\ 72\ hours}{Number\ of\ test\ sites}\ x\ 4\ scoring\ intervals$$

Figure 1. Formula for Primary Irritation Index (PII) [10].

$$\%\ Burn\ Closure\ =\ \frac{Initial\ Wound\ Area - Current\ Wound\ Area}{Initial\ Wound\ Area}\ x\ 100$$

Figure 2. Formula for Burn Closure Percentage [29].

Monitoring of Healing Progression. The treatment was then accompanied by concurrent monitoring of the burn healing progression. The burn wound healing was assessed with the burn closure percentage [9]. A descriptive scoring was also employed to evaluate the redness, swelling, and eschar formation of the burn wound [28].

The healing progression of the burned areas was observed and measured six times (at days 0, 1, 4, 8, 11, and 14) using a digital caliper prior to the application. The daily healing progress was expressed as a burn closure percentage, computed as shown in Figure 2.

Data Analysis. The burn-healing activity of the formulated CNAV hydrogel was evaluated by comparing its burn closure percentage and burn description scores with those of the standard, hydrogel base, and diseased control. A one-way ANOVA at a 95% confidence level was used to determine whether there were significant differences between the groups [9]. If the ANOVA indicated significant differences, Tukey's Honestly Significant Difference (HSD) post hoc test was applied to identify which specific groups differed from one another [30]. This analysis was performed for each scoring day at days 0, 1, 4, 8, 11, and 14.

Results and Discussion

Characterization of Cocos nucifera and Aloe vera. The physical and chemical properties of *Cocos nucifera* and *Aloe vera* were evaluated through organoleptic and quality control testing to evaluate their stability for hydrogel formation.

Homogenized *Cocos nucifera* extract (CNE) displayed a white to off-white color, a mildly sweet odor, and a smooth, creamy texture. In its lyophilized form, the material appeared pinkish-white with a similar odor and a powdery, slightly granular texture. Meanwhile, homogenized *Aloe vera* extract (AVE) exhibited a clear to translucent green color with a mild to slightly bitter odor and a smooth, creamy consistency. Its lyophilized counterpart was light green with a fine powdery texture.

Both the CNE and AVE's properties are consistent with those reported in prior studies and reflect minimal degradation or contamination, confirming the materials' quality and integrity [11, 12].

CNE had an average viscosity of 50,633.33 centipoise (cP), indicating a dense consistency suitable for forming a gel matrix. Its specific gravity was recorded at 1.0205, which falls within the acceptable range of 1.020–1.220 [15], indicating a stable liquid density suitable for topical formulations.

The pH value of 6.17 also falls within the optimal topical pH range (5.56–6.37) [14], indicating skin compatibility and reduced potential for irritation.

AVE showed a lower average viscosity of 784 cp, aligning closely with the standard reference of ~750 cp [17], which supports its utility as a hydrating and spreadable agent in the gel. Its specific gravity was 1.0270, well within the standard range of 1.022–1.032 [16], and its pH was 4.45, which is within the expected range of 4.4–4.7 [13]. The acidic pH may contribute to antimicrobial action and enhanced wound healing, while still being suitable for skin application.

The physical consistency and chemical stability of both raw materials confirm their suitability for hydrogel formulation. The high viscosity of CNE may aid in forming a strong gel matrix, while AVE offers beneficial hydration and wound-healing support. Their complementary properties suggest potential synergy when combined, both structurally (in forming a stable hydrogel) and therapeutically (in promoting burn wound healing).

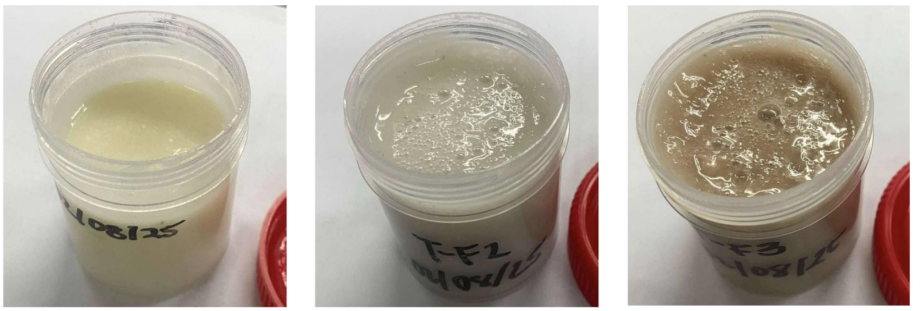
FTIR Analysis of Cocos nucifera, Aloe vera, and Combined. The FTIR spectra of lyophilized *Cocos nucifera*, *Aloe vera*, and their combined extracts revealed the presence of various functional groups, indicating complex phytochemical compositions. C*ocos nucifera* extract (CNE) showed prominent peaks for hydroxyl (O-H) groups at 3350 cm^{-1}, aliphatic C–H groups at 2925 cm^{-1} and 2875 cm^{-1}, and carbonyl (C=O) groups at 1750 cm^{-1}. Similarly, *Aloe vera* extract (AVE) displayed O-H stretching at 3225 cm^{-1}, C–H stretching at 2950 cm^{-1}, and distinct carbonyl-related peaks at 1750 cm^{-1} and 1610 cm^{-1}. The combined extracts exhibited all these characteristic peaks, along with an additional C=C stretching band at 1625 cm^{-1}, suggesting the presence of alkenes or aromatic compounds. These results confirm the coexistence of multiple functional groups, reflecting the rich phytochemical content of both individual and combined plant extracts [31, 32].

Organoleptic Characterization of Combined Cocos nucifera and Aloe vera (CNAV) extracts with Excipients. The organoleptic evaluation of various excipients combined with *Cocos nucifera* and *Aloe vera* (CNAV) extracts demonstrated that all formulations retained their original physical characteristics over 29 days under both refrigerated and room temperature conditions, indicating good compatibility. Powder-based mixtures with excipients such as HPMC, tartaric acid, sodium benzoate, ascorbic acid, potassium sorbate, and acacia gum retained their color, texture, and odor, showing no signs of clumping or discoloration. The samples preserved the characteristic coconut scent, reflecting the stability of the *Cocos nucifera* extract (CNE). Even the semi-solid mixture with glycerin showed no change in appearance or odor, further confirming the physical stability and compatibility of the excipients with the active ingredients.

FTIR Analysis of Drug Excipient Compatibility. FTIR analysis and organoleptic evaluation confirmed the chemical compatibility and stability of all excipients used in formulations containing *Cocos nucifera* and *Aloe vera* (CNAV) extracts [31, 32].

Excipients such as Acacia gum [33], Carbopol [34], glycerin [35], HPMC [36], potassium sorbate [37], sodium benzoate [38], tartaric acid [39], and ascorbic acid [40] showed consistent FTIR spectral profiles over a 29-day storage period, both under refrigerated and room temperature conditions. Characteristic functional group peaks—such as O–H, C–H, C=O, and C=C stretching vibrations—were consistently observed in all samples, with no significant shifts, disappearance, or emergence of new peaks. This indicates the absence of chemical interactions or degradation between the active ingredients and the excipients [18]. Additionally, organoleptic observations confirmed that no changes in color, odor, or texture occurred, further supporting the formulation's physical stability [11,12]. These findings validate that the excipients maintained their structural integrity and are fully compatible with the natural components, making them suitable for stable and effective formulations.

CNAV Hydrogel Formulation Stability. After 7 days of refrigeration, only Formulation 1 remained uniform in color and texture, with no visible aggregates or inconsistencies (Fig. 3 A). Formulations 2 and 3 showed gas formation and color change, indicating degradation. Only Formulation 1 was selected for further testing to confirm stability and efficacy.



A **B** **C**

Figure 3. CNAV Hydrogel formulations after 7 days of refrigeration:
A - Formulation 1; B - Formulation 2; C - Formulation

Table 2. Physicochemical Properties of CNAV Hydrogel Formulation 1 (Day 0 vs Day 30).

Parameter	Day 0	Day 30	Acceptable Range/Reference
pH	6.35	5.42	4.3–6.8 [29]
Spreadability (g·cm/s)	6.45	6.81	6.2–6.9 [30]
Viscosity (cP)	3, 943.3	3,960	<4,000 [47]
Specific Gravity	1.048	1.055	~1.05 [48]
Homogeneity	Uniform	Uniform	No aggregates/phase separation [31]

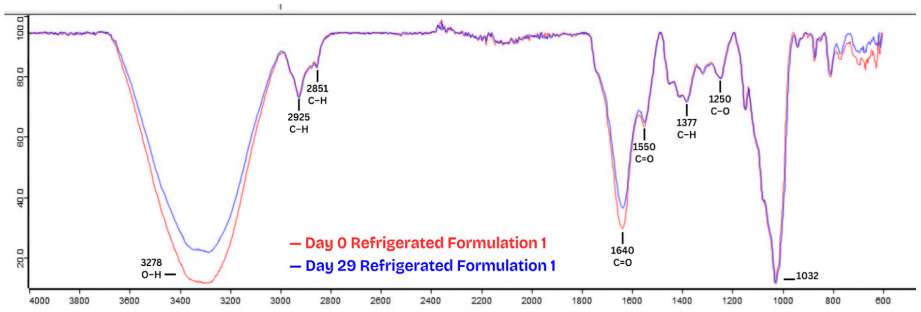


Figure 4. FTIR spectra of CNAV hydrogel formulation 1 on Day 0 and Day 29.

Physicochemical Properties. The physicochemical characteristics of CNAV Formulation 1 were monitored over 30 days of refrigerated storage. The results are summarized in Table 2.

The slight decrease in pH remained within the acceptable topical range of 4.3 to 6.8 [22], indicating good compatibility for skin application. Spreadability remained within the ideal range for dermal products [23], and the increase suggests retained or improved application properties. Viscosity values were within the 3000–4000 cP range recommended for gel formulations [41], ensuring appropriate consistency. The slight increase over the 30-day period may be attributed to water loss. The specific gravity values observed (1.039-1.060) fall within the typical range for hydrogels, around 1.05 [42], although this reference specifically describes PVA-based hydrogels. No existing literature specifically reports the typical specific gravity range for cellulose-based hydrogels, but the comparison suggests that the formulation remains within acceptable limits for topical application.

FTIR Analysis. Fourier-transform infrared (FTIR) spectroscopy was used to evaluate the chemical stability of the hydrogel. Absorption peaks associated with hydroxyl (around 3278 cm^{-1}), aliphatic (2925–2851 cm^{-1}), and carbonyl (1640–1550 cm^{-1}) groups remained unchanged from Day 0 to Day 29. No new peaks or peak shifts were observed, indicating that the formulation did not undergo chemical degradation or interaction. This finding aligns with the observation that consistency in FTIR spectra correlates with chemical stability in plant-based gels [32, 33].

The FTIR and physicochemical findings confirm that the CNAV hydrogel remains stable over time, enabling consistent release and bioavailability of its phytochemicals. This product's stability, reflected in its maintained pH, homogeneity, viscosity, and unchanged FTIR spectral profile, supports the hydrogel's subsequent biological performance. By preserving its structural integrity and preventing premature degradation of its bioactive components, the hydrogel ensures a steady and reliable release of phytochemicals, including polysaccharides, flavonoids, and fatty acids, throughout the treatment period. This sustained availability of active metabolites is essential for modulating inflammation, supporting early epithelial regeneration, and promoting accelerated wound closure [9, 29, 31].

Dermal Irritation Test. Blinded observations for erythema and edema were conducted at 1-, 24-, 48-, and 72-hours following applications of the formulated CNAV hydrogel, hydrogel base, and untreated control on rabbits. No signs of erythema or edema were observed in any test quadrant at 1-, 24-, or 48-hours post-application. At 72 hours, very slight erythema was observed in both sites treated with the formulated hydrogel in one rabbit, while all other sites remained unaffected. The Primary Irritation Index (PII) for the formulated hydrogel was calculated as 1.33, classifying it as a Category 1 (non-irritant) according to the UN GHS 2019 criteria [27]. These results indicate that the CNAV hydrogel formulation is generally well-tolerated and does not induce significant skin irritation in the animal model.

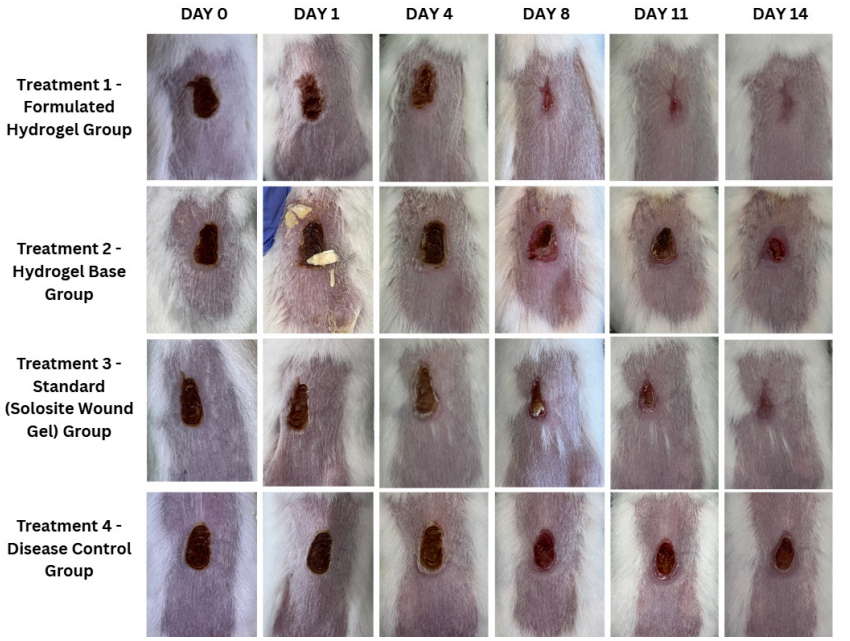


Figure 5. Burn Wound Closure Progression observed in mice treated with CNAV Hydrogel formulation 1, hydrogel base, standard (Solosite Wound Gel), and untreated mice.

Table 3. Burn Closure Percentages Across Treatment Groups.

Day	Treatment 1 (CNAV Formulated Hydrogel)	Treatment 2 (Hydrogel Base)	Treatment 3 (Standard Solosite Wound Gel)	Treatment 4 (Diseased Control)	p-value
0	0	0	0	0	N/A
1	34.20	9.69	20.62	12.66	<0.01
4	45.24	17.75	37.04	25.75	<0.01
8	61.77	42.45	49.57	44.50	0.23
11	71.63	54.20	58.62	54.75	0.31
14	89.60	84.75	93.05	75.48	0.34

Burn Wound Healing Efficacy. The progression of wound healing, as depicted by representative mice, is shown in Figure 5. Table 3 illustrates the progression of burn closure percentages in each of the four groups. The burn closure percentage exhibited significant differences between the groups at Day 1 ($p<0.01$) and Day 4 ($p<0.01$). There were no significant differences in later observations at Day 8 ($p = 0.23$), Day 11 ($p = 0.31$), and Day 14 ($p = 0.34$).

The standard group showed a steady increase in % burn closure until Day 11, followed by a rapid contraction in burn wound areas. By Day 14, the standard group had the highest burn closure percentage among the four groups ($p = 0.34$). The hydrogel base showed slower healing compared to the other groups in terms of burn area contraction, but began to catch up at around Day 8 ($p = 0.23$). The diseased control group exhibited a steady increase in % burn closure, representing the progression of healing without any intervention. Ultimately, it had a lower percentage of burn closure compared to the groups that received intervention; however, this difference on Day 14 was not statistically significant ($p = 0.34$).

Statistical analysis revealed that the CNAV-formulated hydrogel achieved significantly better burn closure than the hydrogel base and diseased control during the early stages (Day 1 and Day 4), but no significant differences were observed at later time points. The convergence in burn closure among all groups from Day 8 onwards may be attributed to natural healing processes. The all-female test population likely contributed to spontaneous healing through estrogen-mediated modulation of inflammation and cell proliferation, thereby diminishing the differences between the diseased control and the treated groups [43, 44]. While the CNAV hydrogel demonstrated promising early burn-healing activity, several limitations should be acknowledged to provide a balanced interpretation of the findings. First, the study used only female BALB/c mice, and estrogen-mediated enhancement of wound repair may have contributed to the rapid spontaneous healing observed across all groups, potentially minimizing differences between treatments at Day 14. In addition, the sample size of n=5 per group, although consistent with common preclinical burn-wound models, limits statistical power and may reduce the ability to detect smaller but clinically meaningful differences in healing responses.

Another limitation is the absence of histopathological analysis, which would have provided deeper insight into re-epithelialization, collagen deposition, angiogenesis, and inflammatory cell infiltration. Such endpoints could verify whether the early improvements in burn closure observed with the CNAV hydrogel translate to true tissue regeneration rather than surface contraction alone. The study also employed a single burn temperature (150°C) and a fixed 14-day observation window, which may not fully represent the variability of real-world burn injuries or capture long-term remodeling phases. These constraints emphasize that, although the CNAV hydrogel showed early therapeutic potential, further studies with larger sample sizes, both sexes, extended time points, and histological confirmation are needed to fully validate its wound-healing efficacy. The comparable efficacy of the CNAV-formulated hydrogel and standard treatment supports the anti-inflammatory and tissue-regenerative properties of *Cocos nucifera* and *Aloe vera* [45, 46]. The significantly better burn closure exhibited by the

CNAV-formulated hydrogel on Day 1 and Day 4 may be due to its modulation of the inflammatory phase and earlier transition to proliferation and re-epithelialization [2].

The superior burn closure observed in the CNAV hydrogel during the early stages may be attributed to the combined bioactive metabolites of *Cocos nucifera* and *Aloe vera.* Both contain flavonoids, polyphenols, vitamins, and polysaccharides with strong antioxidant and anti-inflammatory properties, which regulate inflammation and promote tissue repair [9, 29, 31]. In *Aloe vera*, anthraquinones such as aloin and aloe emodin reduce inflammation, while polysaccharides and glycoproteins enhance fibroblast proliferation and collagen synthesis [47].

Cocos nucifera provides lauric acid, saponins, catechins, and vitamins C and E that scavenge reactive oxygen species, support collagen deposition, and protect against oxidative damage [48, 49]. These compounds strengthen the tissue matrix and facilitate faster epithelial regeneration.

Overall, the flavonoid and polyphenolic metabolites from both plants likely contributed to the CNAV hydrogel's enhanced early healing effect through their antioxidant activity, anti-inflammatory properties, and stimulation of collagen formation.

Conclusion

This study demonstrated that a hydrogel formulated from *Cocos nucifera* endosperm and *Aloe vera* gel offers a promising natural alternative for treating burn wounds. A stable formulation was developed and classified as Category 1 (non-irritant) through patch testing. *In vivo* testing results showed that the CNAV hydrogel significantly accelerated burn wound healing, with closure rates significantly better than those of untreated and hydrogel-based controls. While differences on later days were not statistically significant, the CNAV hydrogel consistently outperformed the negative and diseased control groups, showing healing efficacy comparable to that of a commercial standard (Solosite Wound Gel) throughout the study.

These findings highlight the complementary therapeutic benefits of *Cocos nucifera* and *Aloe vera* CNAV hydrogel in enhancing burn wound closure. The successful development of CNAV hydrogel shows the potential of plant-based wound care products as effective treatment options, particularly in resource-limited healthcare settings. Future research is encouraged to further optimize the formulation, explore long-term outcomes, and evaluate clinical applicability in broader patient populations.

Acknowledgement

The authors would like to express their sincere gratitude to the Faculty of Pharmacy and the Research Center for the Natural and Applied Sciences, University of Santo Tomas, Manila, Philippines.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

ZDAM, MRRM, JTDN, AJSP, KSR, DAER, and ALC made equal contributions to the conceptualization and methodology of the entire manuscript; Data collection ZDAM, MRRM, JTDN, AJSP, KSR, and DAER; Interpretation and analysis of data, ZDAM, MRRM, JTDN, AJSP, KSR, DAER, AMLR, and ALC; original draft preparation, ZDAM, MRRM, JTDN, AJSP, KSR, and DAER; review and editing AMLR and ALC. All authors have read and agreed to the final version of the manuscript.

Institutional Review Board Statement

There were no human participants in the study. All *in vivo* experiments performed were reviewed and approved by the UST Institutional Animal Care and Use Committee with approval number RC2024-451213 dated February 3, 2025.

Informed Consent Statement

Not applicable.

References

[1] Bai, Q., Zheng, C., Chen, W., Sun, N., Gao, Q., Liu, J., Hu, F., Pimpi, S., Yan, X., Zhang, Y., & Lu, T. Current challenges and future applications of antibacterial nanomaterials and chitosan hydrogel in burn wound healing. Materials Advances 2022; 3(17), 6707–6727. https://doi.org/10.1039/d2ma00695b

[2] Markiewicz-Gospodarek, A., Kozioł, M., Tobiasz, M., Baj, J., Radzikowska-Büchner, E., & Przekora, A. Burn Wound Healing: clinical complications, medical care, treatment, and dressing types: The Current State of Knowledge for Clinical practice. International Journal of Environmental Research and Public Health 2022; 19(3), 1338. https://doi.org/10.3390/ijerph19031338

[3] Poncio, M. A. G., & Cruz, J. J. V. Factors associated with mortality, amputation, pneumonia, and skin graft loss among electrical burn patients admitted in a Philippine Tertiary Hospital Burn Center from 2013 to 2019. Burns Open. 2021; https://www.sciencedirect.com/science/article/pii/S2468912221001061

[4] Gupta, A., Kowalczuk, M., Heaselgrave, W., Britland, S. T., Martin, C., & Radecka, I. The production and application of hydrogels for wound management: A review. European Polymer Journal 2019; 111, 134–151. https://doi.org/10.1016/j.eurpolymj.2018.12.019

[5] Kapusta, O., Jarosz, A., Stadnik, K., Giannakoudakis, D., Barczyński, B., & Barczak, M. Antimicrobial Natural Hydrogels in Biomedicine: Properties, Applications, and Challenges—A Concise Review. International Journal of Molecular Sciences 2023; 24(3). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9917233/

[6] Silalahi, J., & Surbakti, C. Burn wound healing activity of hydrolyzed virgin coconut oil. International Journal of PharmTech Research, 2015; 8(1), 67-73. https://www.sphinxsai.com/2015/ph_vol8_no1/2/(67-73)V8N1.pdf

[7] Babu, A., Kumareswari, T., & Malar, T. R. J. J. VEGETATIVE BUD. Environmental Biology: Advanced Research and Multidisciplinary Applications, 2025; 8.

[8] Hekmatpou, D., Mehrabi, F., Rahzani, K., & Aminiyan, A. The effect of Aloe vera clinical trials on prevention and healing of skin wound: A systematic review. Iranian Journal of Medical Sciences, 2019; 44(1), 1-9. https://doi.org/10.30476/ijms.2019.40699

[9] Arollado, E. C., Samaniego, A. A., Agapito, J. D., Tomagan, L. B., Ponsaran, K. M. G., Manalo, R. A. M., & Torre, G. L. T. D. Cocos nucifera L. endosperm promotes healing of excised wound in BALB/c mice. Marmara Pharmaceutical Journal, 2018; 22(1).

[10] Yu, L. X., Amidon, G., Khan, M. A., Hoag, S. W., Polli, J., Raju, G. K., & Woodcock, J. Understanding pharmaceutical quality by design. The AAPS Journal, 2014; 16(4), 771–783. https://doi.org/10.1208/s12248-014-9598-3

[11] Anwar, C., Irmayanti, & Umar, H. A. Characteristics of physical, chemical, and organoleptic properties of virgin coconut oil (VCO) by studying the ratio between coconut cream with inducement oil and length of fermentation. Acta Universitatis Agriculturae et Silviculturae Mendelianae Brunensis, 2020; 68(3), 473–482. https://doi.org/10.11118/actaun202068030473

[12] Aryantini, D., Kristianingsih, I., Kurniawati, E., & Dewanti, T. Formulation, Physical Characteristics, and Irritation Test of Soothing Gel Combination from Aloe vera gel and Dragon Fruit Juice. Indian Journal of Pharmaceutical and Biological Research (IJPBR), 2020; 8(3), 19–25. https://core.ac.uk/download/pdf/335264382.pdf

[13] Guo, X., & Mei, N.. Aloe vera: A review of toxicity and adverse clinical effects. Journal of Environmental Science and Health Part C, 2016; 34(2), 77–96. https://doi.org/10.1080/10590501.2016.1166826

[14] Azra, J. M., Setiawan, B., Nasution, Z., & Sulaeman, A.Effects of variety and maturity stage of coconut on physicochemical and sensory characteristics of powdered coconut drink. Foods and Raw Materials, 2020; 9(1), 43–51. https://doi.org/10.21603/2308-4057-2021-1-43-51

[15] Burns, D. T., Johnston, E., & Walker, M. J. Authenticity and the potability of coconut water - A critical review. Journal of AOAC International, 2020; 103(3), 800–806. https://doi.org/10.1093/jaocint/qsz008

[16] Terry Laboratories Inc. Aloe Vera Gel Reg Inner Leaf 10X. Ultrus. 2016; https://www.ulprospector.com/en/na/PersonalCare/Detail/106783/133730/Aloe-Vera-Gel-Reg-Inner-Leaf-10X

[17] Manna, N. M., & Rudra, N. A. Development and formulation of Aloe vera emulgel. GSC Biological and Pharmaceutical Sciences, 2020; 12(2), 161–166. https://doi.org/10.30574/gscbps.2020.12.2.0262

[18] Pires, H. M., Bastos, L. M., da Silva, E. F., Fonseca, B. B., Sommerfeld, S., de Oliveira Junior, R. J., & Ribeiro, L. N. D. M. Antimicrobial activity of essential-oil-based nanostructured lipid carriers against Campylobacter spp. Isolated from chicken carcasses. Pharmaceutics, 2024; 16(7), 922.

[19] Prasanthi, V., Padmaja, V., & Supriya, Ch. Preparation and evaluation of Aloe-vera hydro-gel containing antibiotic. Research Journal of Pharmacy and Technology, 2020; 13(4), 1961-1964. https://doi.org/10.5958/0974-360X.2020.00353.4

[20] Szulc-Musioł, B., Siemiradzka, W., & Dolińska, B. Formulation and evaluation of hydrogels based on sodium alginate and cellulose derivatives with quercetin for topical application. Applied Sciences, 2023; 13(13), 7826. https://doi.org/10.3390/app13137826

[21] Pandey, P. K., Jain, S. D., Parashar, A. K., & Gupta, A. K. Formulation and evaluation of hydrogel for the treatment of acne. International Journal of Advanced Research in Medicinal Chemistry,2022;4(1),11–15. https://www.researchgate.net/publication/368425757_Formulation_and_Evaluation_of_Hydrogel_for_the_Treatment_of_Acne

[22] El-Kased, R. F., Amer, R. I., Attia, D., & Elmazar, M. M.Honey-based hydrogel: In vitro and comparative In vivo evaluation for burn wound healing. Scientific Reports, 2017; 7(1). https://doi.org/10.1038/s41598-017-08771-8

[23] Abbas, K., Amin, A., Mudassir, J., Alzahrani, A. Y. A., Saher, T., Manzoor, R., Aleem, A., Khan, M. A., Wazir, M. A., Rana, S. J., Khaliq, H. A., Usman, A., Sial, A. S., & Hasnain, S. Z. U. Preparation, characterization and evaluation of hydrogels from different fractions of diverse medicinal plants for management of pain and inflammation. International Journal of Food Properties, 2023; 26(1), 2532–2552. https://doi.org/10.1080/10942912.2023.2250572

[24] Patel, G., Patel, B., Parmar, R., Patel, S., & Nagar, V. A Quality by Design Approach: Development and Evaluation of Herbal Hydrogel. International Journal of Pharmaceutical Sciences and Research, 2023; 14(10). https://doi.org/10.13040/ijpsr.0975-8232.14(10).4810-16

[25] Khan, M., Ware, P., & Shimpi, N. Synthesis of ZnO nanoparticles using peels of Passiflora foetida and study of its activity as an efficient catalyst for the degradation of hazardous organic dye. SN Applied Sciences, 2021; 3(5). https://doi.org/10.1007/s42452-021-04436-4

[26] Charmeau-Genevois, C., Sarang, S., Perea, M., Eadsforth, C., Austin, T., & Thomas, P. A simplified index to quantify the irritation/corrosion potential of chemicals – Part I: Skin. Regulatory Toxicology and Pharmacology, 2021; 123, 104922. https://doi.org/10.1016/j.yrtph.2021.104922

[27] De Andrade, A. L. M., Parisi, J. R., Brassolatti, P., & Parizotto, N. A. Alternative animal model for studies of total skin thickness burns. Acta Cirúrgica Brasileira, 2017; 32(10), 836–842. https://doi.org/10.1590/s0102-865020170100000005

[28] Widyaningsih, W., Yuliani, S., Sofia, V., Rukmiati, R., & Ulwy, K. Burn wound healing activity of ethanol extract gel of Green Algae (Ulva lactuca L) in mice. Pharmaciana, 2022; 12(2), 181. https://doi.org/10.12928/pharmaciana.v12i2.22833

[29] Bello, O. O., Akande, R. O., Bello, T. K., Fashola, M. O., Oni, M. O., & Osho, A. Phytochemical and Antifungal Evaluations of Virgin Cocos nucifera (Coconut) Oil. OBM Integrative and Complementary Medicine, 2025; 10(1), 1-15.

[30] Peck, R., Short, T., & Olsen, C. Introduction to statistics and data analysis. Cengage Learning. 2020.

[31] Rizwana, H., Aljowaie, R. M., Al Otibi, F., Alwahibi, M. S., Alharbi, S. A., Al Asmari, S. A., ... & Aldehaish, H. A. Antimicrobial and antioxidant potential of the silver nanoparticles synthesized using aqueous extracts of coconut meat (Cocos nucifera L). Scientific Reports, 2023; 13(1), 16270.

[32] Ikhou, D., Guendouzi, A., Kaid, M., Ziani, H., Villemin, D., & Chakraborty, A. Preparation and characterization of green adsorbent on functionalized and nonfunctionalized ALOE VERA: A combined experimental and DFT calculations. Journal of the Indian Chemical Society, 2022; 99(7), 100544.

[33] Daoub, R. M. A., Elmubarak, A. H., Misran, M., Hassan, E. A., & Osman, M. E. Characterization and functional properties of some natural acacia gums. Journal of the Saudi Society of Agricultural Sciences, 2018; 17(3), 241–249. https://doi.org/10.1016/j.jssas.2016.05.002

[34] Szabó, B., Süvegh, K., & Zelkó, R. Effect of storage on microstructural changes of Carbopol polymers tracked by the combination of positron annihilation lifetime spectroscopy and FT-IR spectroscopy. International journal of pharmaceutics, 2011; 416(1), 160–163. https://doi.org/10.1016/j.ijpharm.2011.06.028

[35] Andonegi, M., Irastorza, A., Izeta, A., de la Caba, K., & Guerrero, P. Physicochemical and biological performance of Aloe vera-incorporated native collagen films. Pharmaceutics, 2020; 12(12), Article 1173. https://doi.org/10.3390/pharmaceutics12121173

[36] Ding, C., Zhang, M., & Li, G. Preparation and characterization of collagen/hydroxypropyl methylcellulose (HPMC) blend film. Carbohydrate polymers, 2015; 119, 194-201.

[37] Alzate, P., Gerschenson, L., & Flores, S. Study of the performance of particles based on modified starches containing potassium Sorbate and incorporated into biodegradable films: Physicochemical Characterization and antimicrobial action. Chemistry, 2021; 3(2), 658–671. https://doi.org/10.3390/chemistry3020046

[38] Wang, M., Lin, F., Zhao, T., Dong, Y., Hao, X., Ning, D., Zhang, Y., Zhang, K., Zhou, D., Luo, J., Li, X., & Wang, B. The application of a sodium benzoate salt-nucleating agent in recycled polyethylene terephthalate: Crystallization behavior and mechanism. Molecules, 2024; 30(1), 37. https://doi.org/10.3390/molecules30010037

[39] Tsioptsias, C., Matsia, S., Salifoglou, A., Georgiadis, K. E., Kyriakouli, K., Ritzoulis, C., Tsivintzelis, I., & Panayiotou, C. Revisiting the thermal behavior and infrared absorbance bands of anhydrous and hydrated DL-tartaric acid. Molecules, 2025; 30(8), 1732. https://doi.org/10.3390/molecules30081732

[40] Yulia, M., Suhandy, D., Ogawa, Y., & Kondo, N. Investigation on the influence of temperature in L-ascorbic acid determination using FTIR-ATR terahertz spectroscopy Calibration model with temperature compensation. Engineering in Agriculture, Environment and Food, 2014; 7(4), 148-154.

[41] Shiehzadeh, F., Mohebi, D., Chavoshian, O., & Daneshmand, S. Formulation, Characterization, and Optimization of a Topical Gel Containing Tranexamic Acid to Prevent Superficial Bleeding: In Vivo and In Vitro Evaluations. Turkish Journal of Pharmaceutical Sciences, 2022; 20(4), 261–269. https://doi.org/10.4274/tjps.galenos.2022.60687

[42] Sajjan, A., Banapurmath, N., Tapaskar, R., Patil, S., Kalahal, P., & Shettar, A. Preparation of polymer electrolyte hydrogels using poly(vinyl alcohol) and tetraethylorthosilicate for battery applications. IOP Conference Series Materials Science and Engineering, 2018, 376, 012078. https://doi.org/10.1088/1757-899x/376/1/012078

[43] Bird, M. D., Karavitis, J., & Kovacs, E. J. Sex differences and estrogen modulation of the cellular immune response after injury. Cellular Immunology, 2008, 252(1–2), 57–67. https://doi.org/10.1016/j.cellimm.2007.09.007

[44] Horng, H. C., Chang, W. H., Yeh, C. C., Huang, B. S., Chang, C. P., Chen, Y. J., Tsui, K. H., & Wang, P. H. Estrogen Effects on Wound Healing. International journal of molecular sciences, 2017; 18(11), 2325. https://doi.org/10.3390/ijms18112325

[45] Bobiński, R., & Bobińska, J. Fatty acids of human milk – a review. International Journal for Vitamin and Nutrition Research, 2020; 92(3–4), 280–291. https://doi.org/10.1024/0300-9831/a000651

[46] Onggang, F. S., Batbual, B., Romana, A., & Mau, A. Effectiveness of Virgin Coconut Oil (VCO) Topically to The Formation Granulations of Grade I and II Pressure wound (Decubitus). Ahmar Metastasis Health Journal, 2024; 4(1), 20–23. https://doi.org/10.53770/amhj.v4i1.269

[47] Babu, S. N., & Noor, A.Bioactive constituents of the genus Aloe and their potential therapeutic and pharmacological applications: A review. Journal of Applied Pharmaceutical Science, 2020; 10(11), 133-145.

[48] Hu, Y., Hu, L., Zhang, L., Chen, J., Xiao, H., Yu, B., & Pi, Y. Novel electro-spun fabrication of blended polymeric nanofibrous wound closure materials loaded with catechin to improve wound healing potential and microbial inhibition for the care of diabetic wound. Heliyon, 2024; 10(6).

[49] Xu, F. W., Lv, Y. L., Zhong, Y. F., Xue, Y. N., Wang, Y., Zhang, L. Y., Hu, X., & Tan, W. Q. Beneficial Effects of Green Tea EGCG on Skin Wound Healing: A Comprehensive Review. Molecules (Basel, Switzerland), 2021; 26(20), 6123. https://doi.org/10.3390/molecules26206123