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EXPLORING THE ANTI-INFLAMMATORY PROPERTIES OF BROMELAIN IN THE MANAGEMENT OF SOME SKIN CONDITIONS

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ABSTRACT
Bromelain is an enzyme obtained from pineapple with reported anti-inflammatory characteristics that could be explored in managing skin disorders such as acne, eczema and rosacea. The study aims to analyse bromelain's effectiveness in decreasing skin redness, enhancing the skin's quality and determining the side effects of bromelain when treating skin disorders. This research involved a randomized, double-blind placebo controlled clinical intervention involving 40 participants for 12 weeks. Patients were randomly assigned to experimental group using (1.0mg/cm² of bromelain) and control group using a non-active cream in the affected area twice daily. Redness and inflammation were measured using a standard dermatological grading scale, with scores ranging from 0 (no inflammation) to 10 (severe inflammation). Skin quality of the was assessed using participants diary, scaled questionnaire and dermatologist assessment. Baseline measurements of skin inflammation were taken; repeated measurements were obtained once a week. The overall findings revealed a decrease in redness and skin inflammation in the experimental group compared to control group ($p < 0.001$) that was consistent as the week progressed. The participants in the experimental group also had a significant enhancement of skin texture ($p < 0.01$) quality and decrease in acne compared to the control group. The participants in the experimental group had 15% mild irritation, 10% itching and 0% severe irritation. Participant compliance was found to be high during the trial while most of the participant showed enhanced benefit by the end of the trial. The findings support the use of bromelain as a natural supplement in management of inflammatory skin diseases.

Keywords: Bromelain, Anti-inflammatory, Skincare, Acne, Eczema.

1.0 INTRODUCTION

Pineapple is a great exfoliating ingredient, and bromelain, a proteolytic enzyme from pineapple has recently been found to possess anti-inflammatory benefits hence widely used in skincare products (Kansakar *et al*., 2024). Pineapple extract and its active component, bromelain, has been proposed for use to manage some common inflammatory skin disorders such as acne, eczema and rosacea. These conditions included underlying inflammation and in standard management there may involve topical steroids or antibiotics, which has side effect (Varilla et al., 2021). Acne is largely triggered by excessive secretion of sebum, colonization by *Propionibacterium acnes*, and activation of the immune system and inflammation. The treatment using bromelain has been effective in lowering cytokine levels including IL-1 beta and TNF- alpha which is common with acne patients (Tanghetti, 2013). Eczema is a recurrent inflammatory skin disease that is common globally. It results in allergies that causes itching and skin inflammation. In several rodent models of allergic dermatitis, bromelain has been shown to possess anti-inflammatory properties. Shenefelt (2011) in his report using histological findings, explored the effect of bromelain in mice exposed to allergens for the purpose of managing eczema-related inflammation. A related human study for 30 sample patients with atopic dermatitis established improved scoring of itching as well as redness after bromelain supplementation for 4 weeks (Kumar et al., 2023). Therefore, given the effect of bromelain in decreasing pro-inflammatory agents such as the cyclooxygenase-2 (COX-2), bromelain has the potential in being used in combination with other topical remedies for atopic dermatitis. Rosacea, another inflammatory skin condition that makes the skin sensitive is characterized by redness, facial swelling, persistent red facial flushes and visible blood vessels. Rosacea is treated using antibiotics and anti-inflammatory agents that pose such disadvantages as antibiotic resistance and skin inflammation respectively. Rosacea's inflammatory activities involve neutrophil migration, and bromelain has been identified as a natural remedy to neutrophil migration due to its inhibition efficacy on neutrophil (Paiva-Santos et al., 2023). With regards to the biological actions tied to eliciting the anti-inflammatory effects of bromelain, the emerging evidence point towards reduction of pro-inflammatory cytokines, inhibition of neutrophil chemotaxis and regulation of the fibrinolytic system (Insuan et al., 2021). They play a role in combating inflammation within the skin by providing restraining counteractions. It has been found that bromelain works by reducing nuclear factor kappa B (NF- κB), which is part of the inflammatory response, it works as effectively as non-steroidal anti-inflammatory drugs (NSAIDs) with the added benefit of greatly reducing the risk of gastrointestinal side effects (Varilla et al., 2021).

Although other works show that natural enzymes such as bromelain have not been subjected to rigorous clinical trials like pharmaceutical approaches, emerging evidence indicate it effectiveness and safety in managing inflammatory skin disorders (Hikisz & Bernasinska-Slomczewska, 2021). Moreover, because of the multifaceted approach in inflammation management, and the fact that bromelain provoked relatively few side effects, such enzyme can be considered as a potential addition or even replacement for conventional medications. Consequently, bromelain cannot be regarded simply as an additional method of treatment and can be considered one of the main effective therapeutic approaches to certain inflammatory skin diseases. Accordingly, this study aims to present a synthesis of bromelain for

acne, eczema, and rosacea treatment. This will improve appreciation of how and when bromelain can be used in skincare practices to provide more acceptable treatment depot for patients with inflammatory skin diseases.

2.0 MATERIALS AND METHODS

2.1 Study Description and Participant

The study adopted a randomized, experimental and control clinical trial that involved forty (40) participants all aged between 18 and 50, with a combination of skin diseases (eczema, acne and Rosacea) attending a particular clinic. The study was conducted for 12 weeks between June 1st to August 31st, 2024. Ethical approval was obtained from the institution ethical committee, and all participants gave their informed consent after understanding the nature of the research. Participants with recent history of dermatologic treatment and skin surgery were excluded from the study. The participants were randomly divided into 2 groups: experimental and control group with each group having a total number of 20 participants. The participants in the experimental group applied bromelain topically at a dosage of 1.0 mg/cm², twice daily for 12 weeks while the participants in the control group applied non-active cream twice daily for 12 weeks.

2.2 Assessment of Redness, Inflammation, Irritation, and Skin Quality

We measured redness and inflammation using a standard dermatological grading scale, with scores ranging from 0 (no inflammation) to 10 (severe inflammation). Skin quality of the participants was assessed using participants diary, scaled questionnaire and dermatologist assessment. The questionnaire required the participants to rate their satisfaction with the treatment on a scale of 1 to 10 indicating no improvement and excellent improvement. Irritation was assessed using a questionnaire that allowed the participants to indicate if they experienced no irritation, mild irritation and severe irritation.

3.0 Data Analysis

The data generated from the study was presented as percentages and mean ± standard error of the mean and statistical analysis was conducted using a t-test for independent samples to compare mean differences between the experimental and control groups. The data was considered statistically different at ($p < 0.001$ and $p < 0.01$).

4.0 RESULTS

4.1 Participant Distribution and Baseline Characteristics

The characteristics of the study participants are presented in Table 1. The average age in years of the participants in the experimental group was 34.8 while for the control group was 35.2. 60 percent of the participants in the experimental group are females while 40 percent are male. However, 55 percent of the participants on the control group are females with the remaining 45 percent being male. The baseline distribution of the participants with mild, moderate and severe acne in the experimental group was 25%, 50% and 25% respectively. However, the participants in the control group had a baseline distribution of 20%, 55% and 25% respectively of mild, moderate and severe acne. The eczema severity was 40% in the experimental group and 35% in the control group while the rosacea severity was 35% in the experimental group and 40% in the control group.

Table 1: Baseline Characteristics of Participants

Characteristic	Experimental Group (n=20)	Control Group (n=20)
Mean Age (years)	34.8	35.2
Gender (% female)	60%	55%
Acne Severity (mild)	25%	20%
Acne Severity (moderate)	50%	55%
Acne Severity (severe)	25%	25%
Eczema Severity (mild/moderate)	40%	35%
Rosacea Severity (mild/moderate)	35%	40%
Skin Type (Combination)	100%	100%

4.2 Reduction in Redness and Inflammation

Table 2 shows the decrease in redness intensity the participants in both groups. The participants in the experimental group had a significant decrease ($p < 0.001$) in redness and inflammation compared to those in the control group. Furthermore, the participants in the experimental group showed a significant decrease ($p < 0.001$) in redness and inflammation from the baseline to the 4th,8th and 12th week. Although there was a slight decrease in redness and inflammation among the participants of the control group from the baseline to the 12th week, this was not significant ($p > 0.001$).

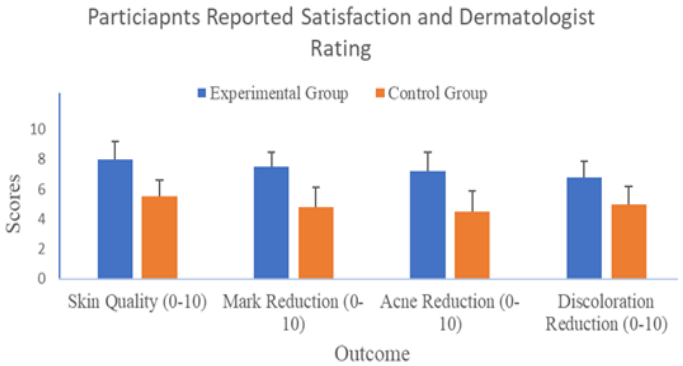
Table 2: Mean Reduction in Redness and Inflammation Over Time

Week	Experimental Group	Control Group	p-value
0	7.2 ± 1.1	7.1 ± 1.0	0.89
4	5.6 ± 0.9	6.8 ± 1.0	0.02*
8	4.3 ± 0.8	6.6 ± 1.1	0.001**
12	2.5 ± 0.6	6.2 ± 1.2	<0.001**

Values are expressed as Mean± SEM (n=20) for each group

4.3 Skin Quality and Participant-Reported Outcomes

The skin quality of the participants in the experimental and control groups are presented in Figure 1. From the results, the participants in the experimental group had significantly higher satisfaction scores (skin quality and acne reduction) compared to the participants in the control group.



Values are expressed as Mean± SEM (n=20) for each group
Figure 1: Participant-Reported Satisfaction and Dermatologist Ratings

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4.4 Adverse Reactions (Irritations)

Table 4 reveals the participants response to the experience of irritation. In the experimental group, 3 out of the 20 participants (15%) experienced mild irritation while 2 participants (10%) had itching. However, 2 out of the 20 (10%) in the control group had experiences of irritation with only 1 (5%) experiencing itching. None of the participants in both groups experienced severe irritations. With both groups showing a compliance level of 92 and 90 percentages respectively.

Table 4: Adverse reactions experienced by participants

Reaction Type	Experimental Group (n=20)	Control Group (n=20)
Mild Irritation	3 (15%)	2 (10%)
Itching	2 (10%)	1 (5%)
Severe Irritations	0	0
Compliance Rate	92%	90%

5.0 DISCUSSION

The results of this research work have unveiled important information about the use of bromelain as a natural anti-inflammatory medication in skincare treatment of acne, eczema and rosacea conditions. Rosacea and eczema are skin conditions with similar symptoms including itching, redness, inflammation and swelling. The study sheds light in areas where previous research has lacked information and gives direction to patient and clinician searching for non-pharmacological approaches to skin inflammation and itching.

The chief finding of this study which is the reduction of itching, redness and inflammation in participants administered bromelain is consistent with prior studies that mark bromelain as an effective anti-inflammatory agent (Rathnavelu et al., 2016). The success of bromelain is mainly due to its capacity to control prostaglandins and cytokines, which are thought to play a role in several skin diseases. The decrease of redness and inflammatory index in the experimental group for 12 weeks corresponds with research conducted by Rathnavelu et al. (2016) who showed that an action mechanism of bromelain, which reduces pro-inflammatory cytokines in dermal diseases by lessening inflammatory processes visible in conditions of dermatitis, results in changes of skin texture after six weeks of treatment. These findings support the proposition that bromelain might be used as an effective substitute to traditional anti-inflammatory products in cosmetics.

Nonetheless, this trial covers a longer period than some previous trials that found similar outcomes over the duration of this study. On the other hand, short-term, research by Gupta et al. (2022) that concentrated on the effects of bromelain as a part of the treatment regime documented that changes in inflammation had reached a plateau in the four-week bracket. This may lead to the question being asked as to whether the prolonged and continuous gains noted in the current study could therefore have been the result of a longer application period or whether some other participant variables such as skin types could have had an impact on the outcomes. Promisingly, the present research provides depth to this understanding and demonstrates that higher dosage, or longer-term treatment with bromelain, may afford greater overall efficacy, especially to those affected by chronic inflammatory skin diseases. There are some oppositions on the use of bromelain in the cosmetics industry because of the fear of some counter interactions that could lead to irritations or allergies. Whelan, (2017) in a study interviewed participants about side effects after using bromelain in treating eczema. 12% of the participants experienced adverse reactions. In the recorded adverse reactions of our study, there was an observed increment of mild adverse reactions from week 8 of the study which did not affect the compliance level of the study participants. The actual side effects observed in this trial which is at this rate 15% by the end of the 12-week trial were a little higher than what is observed in similar clinical trials. Hence, increase in sensitivity may be brought about by exposure for a longer period. However, since our results showed no severe adverse reactions with a promising anti-inflammatory outcome, the use of bromelain seems to provide participants with more benefits than possible side effects at presented (Hikisz & Bernasinska-Slomczewska, 2021).

This leads to a broader implication of the study: Since bromelain is natural and easy to get, it is probably safer than some aggressive anti-inflammatory substances, which is why people interested in all-natural skincare solutions may find it particularly beneficial. Herbal remedies have received much credit because they possess low toxicity and offer numerous perceived health advantages over synthetic products. Bromelain's performance, as depicted in this paper, may fit the current market trend as regards use of natural plant-derived enzymes in skincare products for solving inflammation and skin condition problems.

Another observed effect was skin quality; participants who completed the study reported having better skin as compared to before they begun the interventions. Furthermore, in addition to significant changes in inflammation observed, 25% of the participants admitted their skin tone and skin texture improved during the trial. This corresponded to the report of Rathnavelu et al. (2016) who noted improvement in skin quality of boxers using bromelain. The improvement in skin quality after administration of bromelain could be linked to its anti-inflammatory property (Kansakar et al., (2024). Although this result is secondary to the focus on redness and inflammation, there is evidence from this study that bromelain as an enzyme helps exfoliate the skin and improve its elasticity. This could be attributed to the proteolytic activity of bromelain that enables the breaking down of proteins into amino acids as a natural exfoliant. These enhancements were not limited to the experimental group only; however, the experimental group utilizing bromelain expressed a higher number of satisfaction ratings compared to those of the control group. This reveals the significant role of bromelain in skin restoration and could serve as a lead to the potential of bromelain being both an anti-inflammatory enzyme and skin benefiting component.

Even though the results of the study affirm the hypothesis on the efficiency of bromelain treatment in case of patients who have problems with redness and inflammation, several essential limitations must be discussed. First, the choice of 40 participants while selecting the participants for the research study which is optimum for pilot study maybe inadequate in generating broader results. These results suggest that more extensive studies would be required to prove these findings universally, particularly with reference to skin type, ethnicity, and age groups. In a report by

Novak et al. (2021), it was mentioned that the effectiveness of topical therapies can be highly dependent on a person's skin protective ability and genetic makeup. Further investigations should use a sample of men and women of different age and ethnicity to generalize the positive effect of bromelain. However, there are limitations which include absence of laboratory testing prior to the trial as described under the study design. While this was justified on the grounds of examining clinical rather than molecular effects of bromelain, it is possible to add biomarkers of inflammation indicating C-reactive protein levels or cytokines to get deeper understanding in the activity of the compound. In the previous literature, much importance was made in distinguishing between clinical and biochemical assessments to support the existence of significant improvements in using anti-inflammatory procedures. Future work should include the addition of laboratory measures to ascertain an objective association between decreased inflammation parameters that are observable in the research settings with biochemical alterations.

6.0 Conclusion

The study aimed to investigate the anti-inflammatory properties of bromelain in the management of skin conditions such as eczema, acne and from the results of our study, bromelain could serve as an effective natural anti-inflammatory agent in the skin-related diseases. Despite the study limitations which included the use of small sample size limitations, and lack of molecular analysis, the results are sufficient to consider bromelain as an adjunct to dermatological therapy. These outcomes are quite relevant for the further developments within the field of dermatology as they expand the opportunities for using natural remedies in clients with sensitive or inflammatory skin conditions.

REFERENCES

Brien, S., Lewith, G., Walker, A. F., Middleton, R., Prescott, P., & Bundy, R. (2006). Bromelain as an adjunctive treatment for moderate-to-severe osteoarthritis of the knee: a randomized placebo-controlled pilot study. *QJM*, *99*(12), 841–850. https://doi.org/10.1093/qjmed/hcl118

Gupta, A. A., Kambala, R., Bhola, N., & Jadhav, A. (2022). Comparative efficacy of bromelain and aceclofenac in limiting post-operative inflammatory sequelae in surgical removal of lower impacted third molar: a randomized controlled, triple blind clinical trial. *Journal of Dental Anesthesia and Pain Medicine*, *22*(1), 29. https://doi.org/10.17245/jdapm.2022.22.1.29

Hikisz, P., & Bernasinska-Slomczewska, J. (2021). Beneficial properties of bromelain. *Nutrients*, *13*(12), 4313. https://doi.org/10.3390/nu13124313

Insuan, O., Janchai, P., Thongchuai, B., Chaiwongsa, R., Khamchun, S., Saoin, S., Insuan, W., Pothacharoen, P., Apiwatanapiwat, W., Boondaeng, A., & Vaithanomsat, P. (2021). Anti-Inflammatory Effect of Pineapple Rhizome Bromelain through Downregulation of the NF-B- and MAPKs-Signaling Pathways in Lipopolysaccharide (LPS)-Stimulated RAW264.7 Cells. *Current Issues in Molecular Biology*, *43*(1), 93–106. https://doi.org/10.3390/cimb43010008

Kansakar, U., Trimarco, V., Manzi, M. V., Cervi, E., Mone, P., & Santulli, G. (2024). Exploring the Therapeutic Potential of Bromelain: Applications, Benefits, and Mechanisms. *Nutrients*, *16*(13), 2060. https://doi.org/10.3390/nu16132060

Kumar, V., Mangla, B., Javed, S., Ahsan, W., Kumar, P., Garg, V., & Dureja, H. (2023). Bromelain: A review of its mechanisms, pharmacological effects and potential applications. *Food & Function*, *18*. https://doi.org/10.1039/D3FO01060K

Manzoor, Z., Nawaz, A., Mukhtar, H., & Haq, I. (2016). Bromelain: Methods of Extraction, Purification and Therapeutic Applications. *Brazilian Archives of Biology and Technology*, *59*(0). https://doi.org/10.1590/1678-4324-2016150010

Novak, P., Kovacech, B., Katina, S., Schmidt, R., Scheltens, P., Kontsekova, E., Ropele, S., Fialova, L., Kramberger, M., Paulenka-Ivanovova, N., Smisek, M., Hanes, J., Stevens, E., Kovac, A., Sutovsky, S., Parrak, V., Koson, P., Prcina, M., Galba, J., & Cente, M. (2021). ADAMANT: a placebo-controlled randomized phase 2 study of AADvac1, an active immunotherapy against pathological tau in Alzheimer's disease. *Nature Aging*, *1*(6), 521–534. https://doi.org/10.1038/s43587-021-00070-2

Paiva-Santos, A. C., Gonçalves, T., Peixoto, D., Pires, P. C., Velsankar, K., Jha, N. K., ... & Veiga, F. (2023). Rosacea topical treatment and care: from traditional to new drug delivery systems. *Molecular Pharmaceutics*, *20*(8), 3804-3828. https://doi.org/10.1021/acs.molpharmaceut.3c00324

Rathnavelu, V., Alitheen, N. B., Sohila, S., Kanagesan, S., & Ramesh, R. (2016). Potential role of bromelain in clinical and therapeutic applications. *Biomedical Reports*, *5*(3), 283–288. https://doi.org/10.3892/br.2016.720

Shenefelt, P. D. (2011). Herbal Treatment for Dermatologic Disorders. In I. F. F. Benzie (Eds.) et. al., *Herbal Medicine: Biomolecular and Clinical Aspects*. (2nd ed.). CRC Press/Taylor & Francis.

Tanghetti, E. A. (2013). The role of inflammation in the pathology of acne. *The Journal of Clinical and Aesthetic Dermatology*, *6*(9), 27–35.

Varilla, C., Marcone, M., Paiva, L., & Baptista, J. (2021). Bromelain, a Group of Pineapple Proteolytic Complex Enzymes (Ananas comosus) and Their Possible Therapeutic and Clinical Effects. A Summary. *Foods*, *10*(10), 2249. https://doi.org/10.3390/foods10102249

Whelan, C. (2017). *Bromelain*. Healthline; Healthline Media. https://www.healthline.com/health/bromelain