

Detoxification of the Therapeutically Essential Drug Aelwa (*Aloe vera* (L.) Burm.f.) Using a Modified Traditional Method

Md Aftab Alam¹, Uzma Viquar^{2*}, Ahmed Minhajuddin³, Syeda Hajra Fatima⁴, Mohammad Nawab⁵ and Shayni Khan¹

¹PG Scholar, Department of Ilmul Advia (Pharmacology), National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, T.S, India

²Associate Professor, Department of Ilmul-Advia (Pharmacology), National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, T.S, India

³Director In-Charge, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, T.S, India

⁴Research Officer, Department of Pathology, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, T.S, India

⁵Reader, Department of Moalajat (Medicine), National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, T.S, India

***Corresponding Author:** Uzma Viquar, Associate Professor, Department of Ilmul-Advia (Pharmacology), National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, T.S, India.

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Abstract

In the Unani System of Medicine, drugs are classified into four categories based on their mizaj (temperament). Most medications (first and second degree) are seen to be harmless or safe, however the active principles of some drugs (third and fourth degree) have some adverse consequences, hence these drugs should only be used after thorough *Mudabbar*/detoxification. *Aloe vera* (L.) Burm.f. (*Aelwa*) is a well-known resinous second-degree Unani medicine that is commonly used as a purgative. It is a toxic natural substance that causes gastrointestinal discomfort, cramping, irritation etc. *Mudabbar*/detoxifying is required prior to therapeutic treatment to maximize its efficacy and neutralize its adverse effects.

A literature survey was conducted using online databases (AYUSH Research Portal, PubMed, Scopus, Web of Science, and Google Scholar) with the terms *Aloe vera* OR *Aelwa*, *Aloe barbadensis* OR *Sibr*, *Tadabeer Advia* OR detoxification, *Mudabbar* OR rectification for descriptions of *Aloe vera* (L.) Burm.f. (*Aelwa*). Classical Unani literature were examined for information on detoxification and other aspects of *Aelwa*.

Because the ancient Unanians were fully aware of the negative consequences of the second-degree Unani drug *Aelwa*, they advised using it only after *Mudabbar*/detoxification. After detoxification, the active constituents of *Aelwa* are diluted, and thus the drug's toxicity is mitigated.

Aelwa, as a single medicine or in combination, is useful in the treatment of a variety of human bodily problems. Preparations of *Aelwa* (*Aloe vera* cream) is used in partial thickness burn wounds. In a study it is said that the rate of re-epithelialization and wound healing in the *Aloe*-treated site was much faster than in the silver sulfadiazine-treated site. *Aelwa*, that has been detoxified is more efficient and less harmful. More quality control, preclinical toxicity investigations, and clinical trials are needed to substantiate the ancient Unani Physicians' claims about *Aelwa* detoxification.

Keywords: *Aelwa*; (*Aloe vera* (L.) Burm.f.); *Mudabbar*; *Detoxification*; *Temperament*; *Unani*

Introduction

The Unani System of Medicine is one of the oldest medical systems, having originated in Greece and being brought to India by Arabs and Persians [1]. Regimental therapy (*'Ilāj bi'l-Tadbīr*), Dietotherapy (*'Ilāj bi'l-ghidhā*), Pharmacotherapy (*'Ilāj bi'l-Dawā*), and Surgery (*'Ilāj bi'l-Yad*) are the four major categories of treatment in the Unani System of Medicine [2].

Treatment in the Unani System of Medicine is done with both single and compound medications. The majority of the medications utilized in this medical system are of plant origin [3]. The ancient Unanians were fully aware of the drug's adverse effects and toxicity. Drugs were classified into four categories (1-, 2-, 3- and 4-degree drugs) based on the *Mizaj* (temperament). The first-degree drug causes more coldness/hotness than usual, but it has no effect on the physiological condition, and hotness/coldness can be felt locally. Second-degree drugs create effects that can be examined but are not so powerful that they disrupt everyday routine tasks. Third-degree drugs have effects that can be analyzed and impair normal physiological functioning of the body, but they are not strong enough to cause death. Fourth-degree medications have such severe effects that the physiological functioning of the body is disrupted; these drugs are also deemed toxic [4]. To counteract the harmful effect, medicines are rectified or detoxified. These medications should only be utilized once the *Mudabbar*/detoxification/rectification process has been completed. Otherwise, these medications may disrupt or ruin the body's regular functioning. The medications become physically and chemically pure after the purification process, making them more therapeutically effective and less poisonous [5].

Aelwa is a well-known plant extract derived from the *Aloe vera* (L.) Burm.f. leaf. It is the potent humor phlegm and bile purgative [6-8]. It is *Har* (hot) and *Yabis* (dry) in the second degree, but according to *Ibnsina* *Har* (hot) in second degree and *Yabis* (dry) in the third degree [8,9]. It causes stomach and intestinal distress, as well as cramping and irritation [8]. It should be detoxified as specified in the procedure to lessen its toxicity. The purpose of *Aelwa* detoxification is to neutralize the hazardous principles, convert to the best form for consumption, eliminate undesirable effects such as gastrointestinal irritation and cramping, and increase therapeutic potential [10,11].

Brief description of Saqmonia in light of Unani system of medicine

Aelwa (*Aloe*) has a long history of providing a variety of health benefits and is one of the most commonly used herbal medicines worldwide. There are around 400 *Aloe* species, with *Aloe vera* (L.) Burm.f. (*Aelwa*) being the most widespread and commonly utilized. The name *aloe* comes from the Arabic word *alloeh*, which means "bitter and sparkling material," while the word *vera* comes from the Latin word for "truth" [12]. It is a well-known Unani medication derived from the plant *Aloe vera* (L.) Burm.f., also known as *Aloe barbadensis* Mill., Indian *aloe*, *Kumari*, *Sibr*, *Ghikawar*, and other names [6-8,13]. It belongs to the kingdom *Plantae*, Phylum *Spermatophyta*, Class *Monocotyledonae*, order *Asparagales*, family *Xanthorrhoeaceae*, genus *Aloe* and the species *Aloe vera* [6,14].

Aloe vera has traditionally been used both externally and internally. It is used topically to treat burns, wounds, and skin irritations, and orally to treat constipation, ulcers, diabetes, coughs, headaches, immune system deficiencies, and arthritis. In general, the gel is applied topically to heal wounds, fire burns, and skin irritations, and the latex is known to have cathartic properties. The earliest reported pharmaceutical usage was in ancient Sumeria in 1750 B.C., where it was thought to be a great therapy for stomach irritation and nausea [15].

The majority of *Aloe* species are native to Africa, although they now have a widespread distribution across the world's tropical and subtropical climates. They are grown in warm regions as cultivated and wild plants in nations such as southern, northern, and eastern Africa, China and India [4].

The plant has a coarse appearance, is perennial, shallow-rooted, and has a short stem with leaves connected to it in a rosette arrangement. The plant grows to a height of 30 - 60 cm. The plant contains several tuberous roots and many supporting roots that penetrate the

earth. Aloe flowers are cylindrical and golden in colour. The leaves are densely packed, cuticularized and have a spiky edge. The leaves are made up of a thick layer. Leaves have a thick epidermis (skin) that is covered by a cuticle that surrounds the mesophyll, which contains chlorenchyma cells and thin-walled cells that compose the parenchyma (filet). Mesophyll cells contain *Aloe vera* gel, a translucent mucilaginous jelly. In the pharmaceutical and cosmetic sectors, dried mucilaginous pulp of leaves is employed [6,7,16].

Aelwa is a dried juice of the leaves of *Aloe vera* (L.) Burm.f. [5] obtained by cutting the leaves transversely and draining the liquid, which is yellow and unpleasant in flavor. This liquid is presently evaporated or concentrated by heating and solidified upon cooling, yielding the drug "ALOE" [17].

Aelwa's temperament is Har (hot) and Yabis (dry) in the second degree, whereas according to *Ibnsina*, it is Har (hot) in second degree and Yabis (dry) in the third degree [8,9].

Aelwa contains the following chemical constituents: Arabinans, glucogalactomannan, acidic galactan, polyuronide, cellulose, aloe-emodin, aloin A and B (barbaloin, beta barbaloin, chrysophanol), anthranol, isobarbaloin, capric acid, hexadecadienoic acid, palmitoleic acid, stearic acid magnesium, calcium, zinc, copper, amylase, catalase, echitamine and picrinine [6,7,18].

Pharmacological actions

External action - *Jāli* (detergent), *Muhallil* (Resolvent), *Mujaffif* (desiccant), *Mundamil Qurooh* (wound healer) [9,19,20].

Internally it acts as- *Mushil-i- Balgham* (Phlegmagogue), *Dafe Humma* (antipyretic), *Qatil kirm-e-shikam* (Anthelmintic), *Munaqqi* (evacuant), *Muqawwi-i-Mīda* (stomachic), *Qabiz* (astringent), *Muddir-i Bawl* (diuretic) [7,9,13,20].

Therapeutic use(s)

Aelwa helps in constipation, joint pain and sciatica pain.

Khorasani, *et al.* did a study to compare the efficacy of *Aloe vera* cream to that of silver sulfadiazine for partial thickness burn wounds. The rate of re-epithelialization and wound healing in the Aloe-treated site was much faster than in the silver sulfadiazine-treated site [21].

When applied locally across the forehead with vinegar or *Roghan-e-Gul*, it relieves headaches. It can be used to treat wounds, itching, and all sorts of eye pain. It is beneficial in all sorts of eye pain, including pruritus of the eye, blepharitis, and itching of the eyelids and canthus according to *Hakeem Ibn-e-Hunain*, who agrees with *Dioscorides*. It is also used to treat mouth, nose and ocular inflammation [20].

It treats eye ulcers, dry and moist itching, and all sorts of eye pain, as well as drying out the eye's abnormal humor/*Rutubat*. It acts as a vasodilator and reduces acute inflammation, especially in the vulva. It is useful in tonsillitis, gingivitis, and all other types of inflammation when mixed with honey or alcohol [20].

It is useful in curing tongue inflammation when mixed with honey and alcohol [9].

It is a popular treatment for intestinal worms in children and is used as an anthelmintic enema [22].

It relieves abscesses, especially unclean and diseased ones, and heals moist wounds [20].

It aids in the treatment of ano's hemorrhoid and fissures, and because it has a haemostatic action, it aids in the prevention of bleeding [20].

Its powder both heals and prevents wounds from spreading. It promotes wound healing, promotes the production of scabs, and cures paronychia ulcers. It is used to treat ulcers that are deep and do not heal. It prevents wound secretion as well as resolves accumulated wound secretion [23].

It aids in the healing of the vorheri scar. It is effective for fistulas and non-healing ulcers, particularly around the anus, penis, and nose [9].

Dose of Aelwa

3.5 - 7 gms [8,9].

Leaf pulp juice- 10-20 ml, dried leaf pulp- 125 - 500 mg [19].

Author, Year	Activity	Result
Kumar KPS., et al. 2010 [20], West Dennis P and Ya Fen Zhu., 2003 [24,25]	Burn and wound healing activity	When applied to a wound, <i>Aloe vera</i> boosts both the rate of wound closure and the tensile strength of the wound through cell multiplication. It accomplishes this by increasing the flow of blood to the injured area.
Surjushe, A., et al. 2008; Rajshree, R., 2018 [26].	Moisturizing and anti-aging activity	It increases the skin’s ability to moisturize itself and aids in the elimination of dead skin cells. It accomplishes this by creating collagen and elastin fibres, which make the skin more elastic and less wrinkled, correcting the degenerative skin changes. It softens the skin through its cohesive impact on superficial flaky epidermal cells as well as amino acid action.
Radha, MH and Laxmi Priya, NP, 2014 [27].	Antiviral activity	Prevent viral adsorption and virus replication
Duansak, D., et al. 2003 [28].	Immunomodulation Activity	Increases phagocytosis and stimulates superoxide generation
Langmead, L., et al. 2004 [29].	Antioxidant activity	<i>Aloe vera</i> improves blood quality, most likely by helping the blood to more effectively deliver oxygen and nutrients to the body’s cells.
Reuter, J., et al. 2008 [30].	Anti-inflammatory activity	<i>Aloe vera</i> also inhibits the cyclooxygenase pathway, which reduces the formation of prostaglandins and, as a result, inflammation.
Boudreau, MD, Beland, FA., 2006 [31]	Anti-diabetic activity	The mechanism underlying the reduction in blood glucose levels could be enhanced glucose metabolism or the anti-oxidant impact, which reduces peroxide levels and hence oxidative damage.
Kim, HS., et al. 1999 [32].	Anti-mutagenic activity	By inducing glutathione S transferase and inhibiting the tumor-promoting impact of phorbol myristic acetate, Aloe gel has been demonstrated to play a significant role in chemoprevention.
Bhuvana, KB., et al. 2014 [33].	Effect on gastric acid secretion and ulcers	The lectins (which are controlled by Aloe) block the uptake of aminopyrine by parietal cells. As a result, the extract’s unusual ability to limit gastric acid secretion could be due to direct effect on acid generating cells.
Surjushe, A., et al. 2008 [26].	Antiseptic activity	Lupeol, salicylic acid, urea nitrogen, cinnamomic acid, phenols, and Sulphur are all antiseptic substances found in <i>Aloe vera</i> . They are all antifungal, antibacterial, and antiviral.
Ishii Y., et al. 1994 [34].	Laxative effect	Latex contains anthraquinones, which are powerful laxatives. They accomplish this by raising intestinal water content, promoting mucus secretion, and enhancing intestinal peristalsis.

Table 1: Scientific studies on Aelwa (*Aloe vera* (L.) Burm.f.).

Substitute (*Badal*): Turbud (*Operculina turpethum* (L.) Silva Manso)- half weight of *Aelwa Rasaut* (*Berberis aristata* DC.)- two times weight of *Aelwa* [8,13].

Adverse effects (*Muzir*)

It is toxic to the liver stomach, intestine and the rectum. Excessive use of *Aelwa* causes bloody diarrhoea by causing Sehej (enteritis) and dilation of vessels, and it may also cause haemorrhoids [8,9,20].

Corrective (*Musleh*): *Tragacanth gum* (Kateera), *Rosa × damascena* Herrm (*Gul-e-surkh*), *Pistacia lentiscus* L. (Mastagi), *Commiphora mukul* (Hook. ex Stocks) Engl. (*Muqil*) [8,9,13].

Safety aspect

It is a somewhat harmful natural medicine. Should be used in the quantities specified. To reduce its toxicity, it should be detoxified as described in the next section-methodology [7].

Contraindication(s): Pregnant women were warned not to consume *Aelwa* because its cathartic properties could stimulate uterine contractions, increasing the risk of early labor or miscarriage. Furthermore, nursing mothers should avoid taking laxatives due to the risk of anthraquinones causing diarrhea in their infants [35].

Quality control analysis [7]

1. Name of the drug

- Unani Name: *Sibr* (*Aelwa*)
- Source: Local supplier
- Procurement date: 07/09/2020
- Botanical Name (Family): *Aloe vera* (L.) Burm.f. (Xanthorrhoeaceae).

2. **Makhaz (origin):** Plant.

3. **Part:** Leaf extract.

4. **Form:** Fragmented.

5. **Appearance:** Normal.

6. **Foreign matter:** Nil.

7. **Organoleptic characters:** Blackish brown colour having shiny surface with unpleasant smell and bitter in taste.

8. **Major phytochemicals reported:** Barbaloin.

9. **Quality of drug:** Satisfactory and acceptable.

Materials and Methods

We conducted a thorough review of related articles published in journals using the terms “*Aelwa* OR *Aloe vera*”, “*Aloe barbadensis* OR *Sibr*”, “*Tadabeer Advia* OR detoxification, *Mudabbar* OR rectification” in electronic searches of PubMed, SCOPUS, Google Scholar advanced search, and AYUSH Research Portal for description of *Aelwa* [*Aloe vera* (L.) Burm.f.] and detoxification of herbal drugs. We also conducted manual searches in the NRIUMSD library, Hyderabad, for titles such as *Hippocratic Journal of Unani Medicine*, *Annals of Phytomedicine* etc.

For the Unani concept of *Mudabbar* and the process of *Mudabbar*, as well as the Unani description of *Aelwa*, we assessed several urdu translated copies of traditional Unani literature published by Central Council for Research in Unani Medicine, Idara Kitabus shifa, and others. The most recently recognised name in The Plant List, which is a working list of all plant species, validated the botanical names. <http://www.theplantlist.org>.

Aelwa (*Aloe vera* (L.) Burm.f.) detoxification was completed with minimal adjustments to the detoxification technique given in classical Unani books [36]. The technique was carried out at the Ilmul-Advia National Research Institute of Unani Medicine for Skin Disorders’ Drug Standardization Research Unit (DSRU) in Hyderabad.

Procurement and authentication of study drugs

Aelwa (*Aloe vera* (L.) Burm.f.) was obtained from a local crude drug dealer in Hyderabad; the drug was then recognized and authenticated by the botanist and pharmacognosist at the National Research Institute of Unani Medicine for Skin Disorders in Hyderabad. The authenticated crude drug sample was deposited in the museum of the Survey of medicinal plants unit (SMPU), NRIUMSD, Hyderabad, with the voucher specimen number *Aelwa* (SMPU/CRI-Hyd14243).

Mudabbar/detoxification of Aelwa

With the help of an apple, *Aelwa* was detoxified. This apple was cut down from the bottom and a cavity was formed with a spatula. *Aelwa* was now retained in the apple cavity (about 35 grams of *Aelwa* per 200-gram apple). After this cut part was carefully adjusted to shut the apple and fastened with thread to prevent spilling. The apple was now wrapped in wheat dough and placed in a hot air oven over a petri dish. The temperature was initially set at 80 degrees Celsius for one hour, then reduced to 70 degrees Celsius till the colour of the wheat dough turned brownish red (in next 2 hours). Allow to cool before transferring to the petridish. Dried at room temperature for four days before being placed in a desiccator for the next two days. This processed *Aelwa* is known as *Aelwa Mudabbar* (detoxified *Aelwa*), and the procedure is known as *Tashviya* (Parching).

The detoxifying method mentioned in classical unani literature has been somewhat modified. To achieve homogeneous heating of the apple, a hot air oven was utilised instead of hot ash.

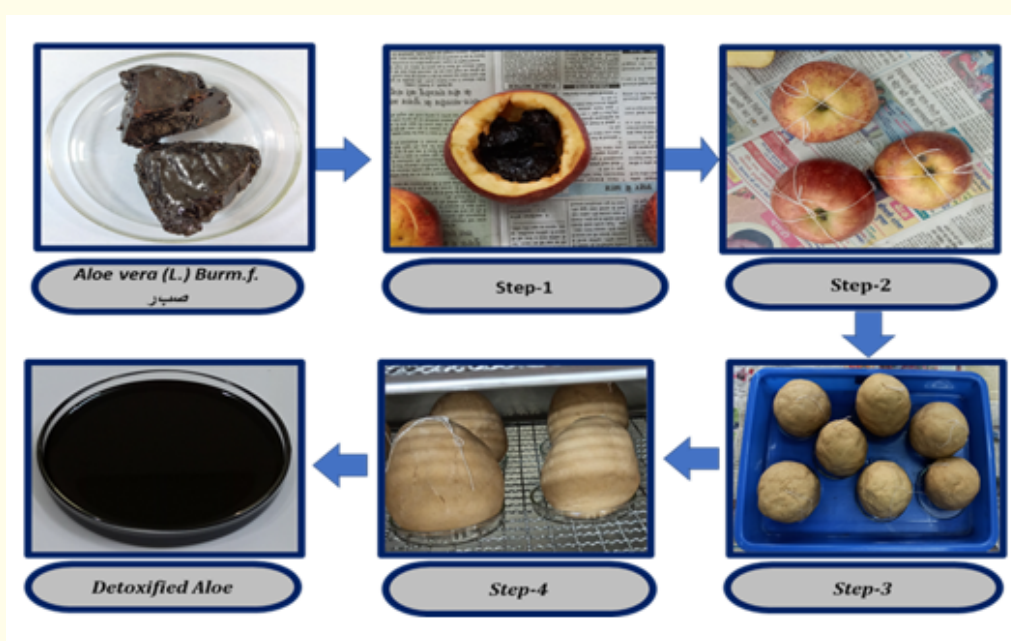


Figure 1: Mudabbar (Detoxification) process of Aelwa (*Aloe vera* (L.) Burm.f.).

Result and Discussion

The general population's use of herbal products is quickly increasing. According to the National Health Interview Survey, nearly 40% of Americans, including adults and children, used complementary and alternative medicine as an alternative therapy in the previous twelve months. Nonvitamin, nonmineral natural products accounted for around \$14.8 billion in purchases, accounting for 44 percent of total out-of-pocket costs for complementary and alternative medicine. Aloe has a long history of delivering a wide range of health advantages, and it is one of the most often used herbal treatments around the world [37].

Aloe contains pharmacologically active chemicals that have been linked to a variety of biological activities such as antiviral, wound healing, antioxidant, anti-inflammatory, laxative, immunomodulating, and anticancer properties. For more than 2000 years, Arab, Chinese, Egyptian, Greek, Indian, Japanese, Korean, and Roman cultures have used *Aloe vera* as a traditional medicine to empirically treat a wide range of disorders and ailments, including skin problems (wounds, x-ray and radium burns, and psoriasis), constipation, external and internal ulcers, hyperlipidemia, diabetes, and lupus erythematosus. Because of the numerous purported benefits, *Aloe vera* production has become an emerging industry for making laxative drugs, cosmetics, and functional food, such as face and hand creams, foundations, cleansers, lipsticks, suntan lotions, shampoos and hair tonics, shaving preparations, bath aids, makeup and fragrance preparations, baby lotions and wipes, yoghurt, drinks, capsules, and tablets [35,38].

Although *Aloe vera* has long been assumed to be a safe functional food ingredient that may be used orally and topically, it has not always been as safe as previously thought. Recently observed deleterious effects in people, as well as toxicity, genotoxicity, and carcinogenicity in both *in vitro* and *in vivo* research, raise concerns about whether *Aloe vera* components may have tumor-promoting actions in humans [39]. Those who are allergic to other plants in the lily family, such as onion and tulips, may experience skin irritation, rashes, cramps, and diarrhea if they take *Aloe vera* topically or orally. There are some case reports on the toxicity or hypersensitivity of Aloe products in humans, but no controlled toxicological studies have been published [40]. After taking *Aloe vera* tablets orally for two weeks before to surgery for leg pain, a 35-year-old lady developed severe intraoperative hemorrhage. *Aloe vera* compounds can reduce prostaglandin synthesis, reducing subsequent platelet aggregation. Sevoflurane, a general anesthetic, inhibits the synthesis of thromboxane A (2) by inhibiting cyclooxygenase activity. Because both sevoflurane and *Aloe vera* have antiplatelet properties, the bleeding could have been caused by herb-drug interaction between the two [41]. After ingesting Cape Aloes, a previously known nephrotoxin, a 47-year-old man had rapid oliguric renal failure and liver impairment [42].

Drugs were classified into four degrees according to the *Mizaj* (temperament): 1°, 2°, 3°, and 4°. Some drugs have certain negative effects on the body; thus, they should only be used after appropriate detoxification/rectification/islah [43].

Because of greater public awareness about the negative effects of conventional medicines, the majority of the developing world's population now employs traditional medicine for wellness [44]. Few drugs of second-degree temperament have been known to contain some hazardous principles such as Jauhar-e-Faal (active principle), thus it is not advisable to fully remove them from the drug. Toxic principles are lowered to an acceptable limit or chemically transformed into nontoxic or less toxic principles during the *Mudabbar*/detoxification process. During the *Mudabbar*/detoxification process, several new principles may be added, which improves the drug's efficacy [45].

According to Devi., *et al.* (2012), Roy., *et al.* (2012), and Srinivasulu., *et al.* (2012), the *Mudabbar* concept of Unani medications is not only for the reduction of poisonous chemicals or unpleasant effects, but also for the enhancement of the drug's efficacy [45-47].

Barbaloin, the active component of *Aelwa*, is a prodrug that is activated by human gut bacteria to aloe-emodin anthrone. Barbaloin, the major laxative component of Aloe, is degraded in the large intestine to aloe-emodin-9-anthrone. Aloe-emodin-9-anthrone is known to

raise the water content of the large intestines, which is a cause of diarrhea. According to the findings of the study, the cathartic action of barbaloin was caused by increased water content in the large intestine and enhanced peristalsis [34].

The effects of heat treatment on barbaloin (a chemical constituent of Aelwa) were studied, and it was discovered that heating caused a significant drop in barbaloin content depending on temperature and duration [48]. When *Aelwa* was retained in apple during the detoxification process, the watery content of apple reacts with chemical ingredients of *Aelwa*, there was rapid breakdown of aloenin, but gradual and slow degradation of barbaloin and aloe-resin [49].

Heating Aelwa at 80°C and 70°C in apple with watery content decreased the content of Barbaloin, resulting in less cramping, irritation, and diarrhea.

Conclusion

Aelwa has a variety of compounds that have both therapeutic and toxicological properties. *Aelwa* and *Aelwa* preparations have been employed as topical and oral medicinal therapies.

The gel is typically used topically to treat wounds and skin disorders, but it can also be used orally to treat gastrointestinal ulcers and diabetes. The FDA regulates latex as a medicine to alleviate constipation, and the whole leaf extract may have antiviral, anticancer, wound healing, antioxidant, laxative, antiseptic and anti-inflammatory properties. *Aloe vera* appears to be safe when used after *Mudabbar* (detoxification). Due to anthraquinones' cytotoxicity, irritation properties, it is critical to monitor the phenolic component concentration of *Aloe vera* whole leaf extract and latex.

According to the International Aloe Science Council standard, the maximum permissible aloin content in Aloe-derived material for oral consumption should be less than 10 ppm (parts per million); for nonmedical use, the recommended limit is 50 ppm or lower.

Mudabbar/rectification/detoxification of *Aloe vera* (L.) Burm.f. (*Aelwa*) as mentioned in Unani System of Medicine is performed to reduce hazardous chemical contents or metabolites. However, the *Mudabbar* procedure has not been scientifically validated by the Unani system of medicine.

Because of the rising popularity and use of the Aloe, more research is needed to explore the adverse effects, drug interactions, and potential toxic effects of *Aelwa* and *Aelwa* preparations, particularly after long-term use of these products before and after the detoxification process.

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Conflict of Interest

None.

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