Pharmacological Effects and Pharmaceutical Dosage Forms Development of *Aloe vera*

Jamal Nasser Saleh Al-maamari
Postgraduated Study Program, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

Tanaman lidah buaya merupakan salah satu tanaman tertua yang digunakan selama ribuan tahun. Lidah buaya telah digunakan sebagai ramuan yang menyembuhkan berbagai penyakit sepanjang sejarah. Sejumlah penelitian yang dilakukan dalam dua dekade terakhir menjelaskan sifat kimia dan senyawa alami yang terkandung dalam tanaman ini, seperti antrakuinon, asam amino, acemannan, aloesin, dan glukomanan, yang menunjukkan efek terapeutik yang beragam. Artikel ini bertujuan untuk meninjau efek farmakologis tanaman lidah buaya dan berbagai bentuk sediaan farmasinya. Data dikumpulkan dari literatur internasional yang diterbitkan di PMID dan Google Scholar. Dapat disimpulkan bahwa lidah buaya memiliki berbagai efek terapi seperti anti inflamasi, penyembuhan luka, anti oksidan, anti kanker, anti tumor, anti tukak, antivirus dan antibakteri, serta anti kolesterol. Selain itu, beberapa formulasi farmasi *Aloe vera* dapat disiapkan selama pengembangan produk, termasuk supositoria, krim, gel, dan tablet.

Kata kunci: Lidah buaya; bentuk sediaan farmasi; efek farmakologis; pengembangan produk.

The *Aloe vera* plant is one of the oldest plants used for thousands of years. *Aloe vera* has been used as a herb that cures multiple diseases throughout history. Numerous studies conducted in the past two decades shed light on the chemical properties and natural compounds contained in this plant, such as anthraquinone, amino acids, acemannan, aloesin, and glucomannan, exhibiting diverse therapeutic effects. This article aimed at reviewing the pharmacological effects of *Aloe vera* plant and its different pharmaceutical dosage forms. Data were collected from international published literature in PMID and Google Scholar. It can be concluded that the *Aloe vera* has various therapeutics effects such as anti-inflammatory, wound healing, anti-oxidant, anticancer, anti-tumor, antiulcer, antiviral and antibacterial, and anti-cholesterol. In addition, some pharmaceutical formulations of *Aloe vera* can be prepared during product development, including suppositories, creams, gels, and tablets.

Key words: *Aloe vera*; pharmaceutical dosage forms; pharmacological effects; product development.

*Corresponding author: Jamal Nasser Saleh Al-maamari, Postgraduated Study program, Faculty of Pharmacy. Universitas Airlangga, Surabaya, Indonesia

INTRODUCTION

Aloe vera comes from the Latin word "true aloe," and this is attributed with the versatility, many health benefits and therapeutic effects of these Aloe species (Gage, 1996). *Aloe vera* (*Aloe vera* L.) is a familiar plant because it is known to be suitable for hair care and is a horticultural plant that has been known for a long time. However, only a few people know its benefits and properties. Yet, since ancient times, this plant is known to occupy an essential place in the medical field and it is known as a plant of immortality, a royal plant, and is considered a gift from God. One of the queens of ancient Egypt, namely Cleopatra, used *Aloe vera* regularly for her beauty. Queen Nefertiti also uses *Aloe vera* to treat her skin and maintain her digestive health (Brandon, 2015).

Aloe vera is native to Africa, precisely in Ethiopia, which belongs to the Liliaceae family. The shape of this plant's stem is short with a spear-like form. The leaves' shape is upright, and the edges are lined with thorns but not so sharp. This *Aloe vera* leaf is waxy green and has thick, clear flesh inside. *Aloe vera* itself has a unique feature, namely its ability to survive in dry areas during the dry season, by closing its stomata tightly. Thus this plant is very suitable to be cultivated in Indonesia (Malik *and* Zarnigar, 2013).

Parthasarathy *et al.* (2017) conducted a research related to the qualitative test of phytochemical compounds in *Aloe vera* extract. They reported that *Aloe vera* extract contains flavonoids, steroids, anthraquinones, phenols, tannins, and carbohydrates. These compounds are responsible for the pharmacological activity of *Aloe vera*. Based on a study reported by Attah *et al.* (2016), *Aloe vera* gel can be used for wound healing and reducing the inflammed tissues. In addition, *Aloe vera* has been prepared in various pharmaceutical products, including topical O/W cream (Akhtar *et al.*, 2011). This cream may give a moisturizing effect on the skin and reduce the TEWL (Transepidermal water loss) rate.

This review aims to provide information about the pharmacological activity and product development of *Aloe vera* in the pharmaceutical field, based on a literature study. Until now, several studies have discussed the use of *Aloe vera* as an anticancer, antioxidant, antimicrobial, and anti-inflammatory. Since there are plenty of previous and recent articles discussing about the medical aspect and medical benefits of *Aloe vera* plant extract, this present review is novel as it addressed the recent updates of the therapeutic benefits and pharmaceutical dosage forms or preparations of *Aloe vera* plant extract.

In this review article, the data presented were obtained from online published international literature in PMID and Google Scholar.

A. Pharmacological Activities

1. Anti-inflammatory

Inflammation is the body's response to tissue injury and infection. When inflammation occurs, there is a vascular reaction in which fluids, blood elements, white blood cells, and chemical mediators gather at tissue injury or infection site. Inflammation is the body's protective mechanism that attempts to neutralize and eradicate harmful agents at the injury site and prepare the environment to repair the tissues. The main signs of inflammation are redness (erythema), swelling (edema), heat, pain, and loss of function (Paul *et al.*, 2014)

The presence of sterols, anthraquinones, and other natural substances, including polysaccharides in *Aloe vera*, work synergistically to cause anti-inflammatory effect (Barcroft *and* Myskja, 2003). According to research conducted by Hu *et al.* (2003), *Aloe vera* has antioxidant enzymes that can inhibit inflammatory mediators and act as pain relievers. This study used albino male rats which were incised on the back, causing wounds. Reduced redness (erythema) intensity in the treatment group was observed significantly faster than in the control group. The decrease in the reddish color intensity of erythema is thought to be associated with the presence of ascorbate-dependent peroxidation and catalyst enzymes contained in *Aloe vera* water extract, which may inhibit the cyclooxygenase pathway. This confirms that *Aloe vera* water extract has anti-inflammatory activity.

2. Wound Healing

The term wound refers to a condition where normal skin is damaged, although the severity and depth of wound may vary widely. The wound includes a tear or laceration in the skin layer (open wound) and bruising from being hit by a blunt object (closed wound). However, in pathology, the term wound is limited to cases of trauma that occur in skin structures, having penetrated the epidermis and caused damage to the skin dermis (Moriyama *et al.*, 2016).

Aloe vera is known to have the ability to heal wounds. Based on a research conducted by Hashemi *et al.* (2015), *Aloe vera* demonstrates a good effect on wounds, by reducing inflammation significantly and providing more mature granulation tissue, which plays a role in accelerated wound healing. The administration of *Aloe vera* gel also thickens the epithelial layer. The blood supply to the dermis was also increased compared to the control group, as well as accelerating the migration of fibroblasts to the wound area.

Ramz *et al.* (2016) also carried out a study related to the effectiveness of aloe extract in wound healing of male Wistar rats. The results of this study indicated that the aloe extract concentrations of 1.5% and 2% were effective in the treatment of burn wound healing, compared with the other concentrations.

3. Antibacterial, Anti-fungal, and Antivirus

Antibacterial agent is given to treat infectious diseases, but it may encourage resistance to the given antibacterial agent if the use of this agent is not controlled. The bacterial growth inhibition is assumed to be caused by the interaction of phenol compounds that bind proteins in bacteria to form bacterial complexes via unspecific bonds. *Aloe vera* is a medicinal plant that has antibacterial properties. A research result on *Aloe vera* leaf bark extract reported by Rivandi *et al.* (2012), concluded that it contains a number of identified active substances including saponins, sterols, and acemannan, which can inhibit the growth of *Staphylococcus aureus* and *Escherichia coli* bacteria.

Hussain *et al.* (2015) evaluated the *in vitro* antibacterial activity of *Aloe vera* using the agar diffusion method on a plate. It was reported that *Aloe vera* is effective against *Streptococcus mutans* and *Lactobacillus casei*. To confirm its antibacterial activity, *Aloe vera* was also tested together with *Ocimum sanctum*. It was observed that they both act synergistically and are effective against *S. mutans* and *L. casei* bacteria. Based on this research result, the anthraquinones and saponins contained in *Aloe vera* leaves are directly responsible for the antibacterial activity, while the polysaccharides also have an indirect antibacterial activity, as it will stimulate the phagocytosis of leukocytes to destroy bacteria.

Apart from having antibacterial activity, *Aloe vera* also has anti-fungal activity. A research conducted by Shireen *et al.* (2015) evaluated *Aloe vera* leaf extract's *in vitro* ability to inhibit the growth of the fungus *Candida albicans* that is responsible for candidiasis. It was observed that *Aloe vera* displayed an excellent anti-fungal effect on *C. albicans*, and the inhibitory effect varied with the concentrations of *Aloe vera* leaf extract. The extract concentration of 1000 µg/ml of *Aloe vera* extract had inhibition capability equivalent to 10 µg amphotericin B. The compounds contained in *Aloe vera* extract have anti-fungal substances, which are saponins and acemannan. Another study conducted by Ortega-Toro *et al.* (no date) reported the activity of *Aloe vera* gel against six fungi (*Fusarium oxysporum*, *Alternaria alternate*, *Colletrotrichum gloesporoides*, *Bipolaris spicifera*, *Curvularia hawaiiensis*, and *Botryotinia fuckeliana*) causing disease in plants. The result of this study showed that *Fusarium oxyporum* is the most sensitive fungus to *Aloe vera* gel.

Other study carried out by Zandi *et al.* (2007) also stated that *Aloe vera* has an antiviral activity that is believed to be derived from anthraquinone compounds. The research results showed that the *Aloe vera* plant-derived from Bushehr has good potential as a natural source of medicinal ingredients to fight against the herpes simplex virus type 2.

4. Antioxidants

Antioxidants are closely related to free radicals. Free radicals are an atom, group, molecule, or compound that can contain one or more non-double electrons in the outer shell. Therefore free radicals have very high reactive properties, which tend to attract electrons. In addition they have an ability to convert the molecule into new free radicals, yielding a chain reaction. This new chain reaction can be terminated when the free radicals are inhibited by antioxidants. Thus, antioxidants are compounds that can delay, slow down, and prevent the oxidation process originated from free radicals (Mathew *et al.*, 2011).

Aloe vera is a plant that has strong antioxidant activity, thus helping the body fight against free radicals (cancer-forming agents) through the actions of antioxidant compounds, including vitamins A, C, and E, as well as other nutrients (Barcroft and Myskja, 2003).

Miladi and Damak (2008) evaluated the complete antioxidant and phenol activity of hexane, ethyl acetate, chloroform-ethanol, and butanol fractions of ethanol extract from *Aloe vera* bark, in order to assess the antioxidant activity of *Aloe vera*. The chloroform-ethanol fraction showed the highest total phenol, followed by ethyl acetate, butanol, and hexane fractions. However, the hexane fraction showed the largest antioxidant capacity when tested by the phosphomolybdenum and β-carotene bleaching methods. In contrast, the highest antioxidant activity was the chloroform-ethanol fraction when evaluated by the DPPH method (2,2-diphenyl-1-picrylhydrazyl).

5. Anticancer

Cancer is a disease characterized by an uncontrolled division of cells and these cells' ability to invade other biological tissues. *Aloe vera* is known to have the effect of inhibiting the growth of cancer cells due to aloesin, aloe-resin, and aloe-emodin. A study conducted by Putri and Medawati (2016) states that the ethanol extract of *Aloe vera* is effective in inhibiting the proliferation of SP-C1 cells (solid cancer in the oral cavity) *in vitro*, using SP-C1 cancer cell cultures cultured in Dulbecco's modified eagle medium (DMED) given fetal Bovine Serum 10% (FBS). It is known that aloe-emodin in *Aloe vera* at specific doses can inhibit the growth of oral cancer cells. The most effective concentrations in inhibiting the proliferation of SP-C1 cells were

reported to be 75 mg/ml and 100 mg/ml. The inhibition mechanism in the growth of SP-C1 cells occurs by inhibiting the cell cycle in the G2 phase.

Another study was also conducted by Hussain *et al*. (2015). They analysed the inhibition activity of *Aloe vera* extract against the proliferation of breast and cervical cancer cells, and examined its synergistic effect along with cisplatin. It is established that *Aloe vera* used, either with or without cisplatin, has an antineoplastic effect on breast and cervical cancer by causing apoptosis and modulating effector molecules.

6. Anti-tumor

Aloe vera also has anti-tumor activity. Naveena (2011) evaluated the anti-tumor activity of 50% (100 mg/kg) ethanol extract of *Aloe vera* against Ehrlich Ascites Carcinoma (AEC) in Swiss albino mice. *Aloe vera* activity showed decreased abdominal circumference and the weight of AEC tumors in mice. It is known that the treatment with *Aloe vera* can restore serum biochemical parameters to normal levels and reduced levels of lipid peroxidation, as well as increased levels of reduced glutathione and other antioxidant enzymes (SOD, CAT, and GPx). Thus, 50% of the tested *Aloe vera* ethanol extracts showed anti-tumor effects by modulating lipid peroxidation and increasing the AEC tumors' antioxidant defense system. In addition, treatment with *Aloe vera* exhibited significant inhibition of metastases in the liver and lymphatics and showed antimetastasis activity, supported by anti-tumor and hepatoprotective activity. Thus, the synergistic antioxidant activity owing to phytochemical compounds such as flavonoids, triterpenoids, steroids, which is present in *Aloe vera*, might be responsible for its anti-tumor activity.

7. Anticholesterol

Evaluation of *Aloe vera* juice's effect on HDL and LDL cholesterols in people with dyslipidemia was conducted by Sianipar and Isnawati (2012). This study reported that the consumption of *Aloe vera* juice at a concentration of 200 mg/day for 14 days may reduce LDL cholesterol level by 20.36% and increase HDL cholesterol level by 18.87%. *Aloe vera*'s contents, which is thought to reduce LDL (Low-Density Lipoprotein) cholesterol and increase HDL (High-Density Lipoprotein) cholesterol, is a water-soluble fiber, are glucomannan, antioxidants, flavonoids, niacin, vitamin C, magnesium, selenium, and zinc.

8. Antiulcer

A research to examine the effect of *Aloe vera* on indomethacin-induced ulcer in albino Wistar rats and its comparative effect with omeprazole given intraperitoneally was conducted by Borra *et al*. (2011). Indomethacin was given orally at a dose of 20 mg/kg BW. The *Aloe vera* dosage form administered orally to mice was *Aloe vera* powder mixed with acacia gum, dissolved in distilled water. The observed parameters were changes in the histology of rats' stomach. It was concluded that *Aloe vera* has an antiulcer activity that is statistically comparable with the drug omeprazole. Thus, *Aloe vera* has cytoprotective properties and may reduce stomach acid-like omeprazole.

B. Product Development

1. Nanoparticles

The development of products containing *Aloe vera* has been carried out. One of the developed products is nanoparticle preparation. Kassama and Misir (2017) evaluated the morphology, physiochemistry, and controlled release of nanoparticles synthesized with Poly (lactic-co-glycolide acid) or PLGA for nanoencapsulation of *Aloe vera*. *Aloe vera* freeze-dried samples were used in this study. The nanoparticles were prepared using ultrasonication solvent evaporation technology. The freeze-dried *Aloe vera* gel powder and liquid *Aloe vera* gel nanoparticles exhibited bioactive release kinetics, regulated by a combination of mass diffusion and capillary actions. Parthasarathy *et al*. (2017) has also prepared synthesized nanoparticles from ZnO containing *Aloe vera* leaf extract, and was then evaluated for its antibacterial activity. It was concluded that the synthesis of ZnO nanoparticles derived from *Aloe vera* extract has good antibacterial activity against *Staphylococcus aureus* and *Salmonella typhi*.

2. Tablets

Aloe vera extract has also been formulated as tablet dosage form. Kasmawarni and Utomo (2010) developed effervescent tablets containing *Aloe vera* extract. The maceration process was employed to prepare *Aloe vera* extract. The best *Aloe vera* extract effervescent tablet formula, contains 150 mg *Aloe vera* extract granules, 1890 mg lactose, 100 mg citric acid, 300 mg tartaric acid, 400 mg sodium bicarbonate, 60 mg PEG-6000, 100 mg aspartame, and flavour to taste.

Another study was also conducted by Singh *et al*. (2012). They designed the Gastroprotective Drug Delivery System (GGDS) formulation. The GDDS contained two active substances for antiulcer activity, namely *Aloe vera* and alginate. It was concluded that this tablet preparation exhibited the enhanced pharmacological effect of *Aloe vera*-alginate.

Furthermore, Rathod *et al*. (2015) developed *Aloe vera* preparations for chronic periodontitis. The formulation used for *Aloe vera* chips include: 5% *Aloe vera*, 600 mg hydroxy

propyl cellulose, 100 mg hydroxy propyl cellulose, 50 mg polyethylene glycol, 10 ml water (q.s.). The chip dimensions were 4 mm long, 2 mm wide, and size 0.3 mm. The *Aloe vera* chips have been checked on 20 topics and it confirms that *Aloe vera* chips may enhance periodontal status.

3. Suppositories

Kawan-kawan (2016) has developed suppositories formulation containing purified extract of *Aloe vera* leaves. *Aloe vera* extract was poured into the suppository base, namely oleum cacao and Cera Alba (beeswax) as well as PEG 400 and PEG 4000. It was reported that the best physical properties of suppository was observed in the formula utilizing a coconut oil base with the addition of 4% cera alba, 50% PEG-400, and 50% PEG-6000 base suppository.

4. Gel and Cream

Aloe vera has also been developed as a topical preparation. The development of gel preparation has been conducted by Galeri *et al.* (2016), who studied the effect of Na CMC on the physical quality of *Aloe vera* extract gel. The formula containing 5% Na CMC exhibited the most influential physical quality of *Aloe vera* gel. It was concluded that the *Aloe vera* gel formulation with good physical quality contains 10% *Aloe vera* extract, 5% Na CMC, 0.2% Nipagin, 2% TEA, 25% glycerin, and up to 100% distilled water. Other study has been conducted by comparing the effectiveness of *Aloe vera* gel and povidone-iodine on the performance of mice skin incisions. This study indicated that the topical administration of *Aloe vera* gel has a more beneficial effect than that of povidone-iodine in stimulating epithelialization, fibroplasia, and blood vessel formation. The wound-healing effect of *Aloe vera* may be associated with its acemannan content. This compound may act as a potent agent that activates macrophages (a key role in tissue repair regulation). Macrophages will also release cytokines and growth factors (PDGF, TDF-a, TGF-β, EGF VEGF), which will recruit fibroblasts, keratinocytes, and endothelial cells to repair tissue (Athavale *et al*., 2017).

Another product development of *Alove vera* extract is *Aloe vera* cream, carried out by Akhtar *et al.* (2011). The developed the product and subsequently evaluated the pharmaceutical effect of *Aloe vera* cream. The prepared W/O or O/W type of cream contained an oil phase, consisting of paraffin oil (16%) and surfactant ABIL-EM 90 (4%), as well as the water phase, consisting of *Aloe vera* extract (3%) and distilled water (as sufficient). The developed cream product was tested on 21 subjects, given to the cheeks for eight weeks. The parameters measured weekly in this study were the water content in the stratum corneum and Transepidermal Water Loss (TEWL). The prepared formulation may increase the moisturizing effect or moisture on the skin and reduce TEWL in dry skin.

Aloe vera cream preparation, when compared to silver sulfadiazine, shows better antimicrobial activity. *Aloe vera* cream may inhibit the growth of Gram-negative organisms such as *Escherichia coli*, *Enterobacter cloacae*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa*. Additionally it may also inhibit the growth of Gram-positive organisms such as *Staphylococcus aureus*, *Streptococcus pyrogens*, *Streptococcus agalactiae*, *Streptococcus faecalis*, and *Bacillus subtilis* (Barcroft and Myskja, 2003).

CONCLUSION

Aloe vera L. has numerous pharmacological activities. It plays a major role in wound healing. It may also act as an anti-inflammatory, antibacterial, anti-fungal, antiviral, antioxidant, anticancer and anti-tumor, anticholesterol, and antiulcer agents. As one of the pharmaceutical products, *Aloe vera* has also been exposed to great product developments. It has been developed in various pharmaceutical dosage forms such as nanoparticles, tablets, suppositories, gels, and creams.

ACKNOWLEDGEMENT

I thank Dr. Mahardian Rahmadi for his support during the research and also to all persons who offer technical support during data collection and analysis.

REFERENCES

Akhtar, N. *et al.* 2011. 'Formulation development and moiturising effects of a topical cream of *Aloe vera* extract', *World Academy of Science, Engineering and Technology*, 51, pp. 172–179.

Athavale VS, Shivmurti N. Khandalkar, Megha Mahawar, Iresh Shetty, Aditya Lad Athavale, V. S. 2017. 'A comparative study between *Aloe vera* gel dressing and conventional dressing in chronic wounds', *International Surgery Journal*, 4(10), pp. 3427–3432.

Barcroft, A. and Myskja, A. 2003. Aloe vera: Nature's silent healer. Alasdair AloeVera.

Borra, S. K., Lagisetty, R. K. and Mallela, G. R. 2011 'Anti-ulcer effect of *Aloe vera* in non-steroidal anti-inflammatory drug induced peptic ulcers in rats', *African Journal of Pharmacy and Pharmacology*, 5(16), pp. 1867–1871.

Brandon. 2015. The Everything Guide to Aloe Vera for Health: Discover the Natural Healing Power of *Aloe Vera*: Brandon, Britt: 0045079586949: Amazon.com: Books. Available at: https://www.amazon.com/Everything-Guide-Aloe-Vera-Health/dp/1440586942 (Accessed: 15 August 2020).

Gage, D. 1996. *Aloe vera*: Nature's soothing healer. Inner Traditions/Bear & Co.

Galeri, T. I., Astuti, D. S., and Barlian, A. A. 2016 'Pengaruh jenis basis CMC Na terhadap kualitas fisik gel ekstrak lidah buaya (*Aloe vera* L.)', *Parapemikir: Jurnal Ilmiah Farmasi*, 4(1), pp. 25 – 29.

Hashemi, S. A., Madani, S. A., and Abediankenari, S. 2015. 'The review on properties of *Aloe vera* in healing of cutaneous wounds', *BioMed Research International*, Volume 2015: Article ID 714216, https://doi.org/10.1155/2015/714216

Hu, Y., Xu, J., and Hu, Q. 2003. 'Evaluation of antioxidant potential of *Aloe vera* (*Aloe barbadensis* Miller) extracts', *Journal of Agricultural and Food Chemistry*, 51(26), pp. 7788–7791.

Hussain, A. *et al.* 2015 'Aloe vera inhibits proliferation of human breast and cervical cancer cells and acts synergistically with cisplatin', *Asian Pacific Journal of Cancer Prevention*, 16(7), pp. 2939–2946.

Kassama, L. S. and Misir, J. 2017. 'Physicochemical properties and control release of *Aloe vera* (*Aloe barbadensis* Miller) bioactive loaded poly (lactic co-glycolide acid) synthesized nanoparticles', *Advances in Chemical Engineering and Science*, 7(04), p. 333.

Kawan-kawan, N. 2016. Formulasi dan Evaluasi Suppositoria Ekstrak Terpurifikasi Daun Lidah Buaya (*Aloe vera*), Acta Pharmaciae Indonesia. 4(1) 7-14.

Malik, I. and Zarnigar, H. N. 2013 'Aloe vera-A review of its clinical dffectiveness', *International Research Journal of Pharmacy*, 4(8), pp. 75–79.

Mathew, B. B., Tiwari, A., and Jatawa, S. K. 2011. 'Free radicals and antioxidants: A review', *Journal of Pharmacy Research*, 4(12), pp. 4340–4343.

Moriyama, M., Hiroyuki Moriyama, Junki Uda, Hirokazu Kubo, Yuka Nakajima, Arisa Goto, Junji Akaki, Ikuyo Yoshida, Nobuya Matsuoka, Takao Hayakawa. 2016. 'Beneficial effects of the genus Aloe on wound healing, cell proliferation, and differentiation of epidermal keratinocytes', *PloS One*, 11(10), p. e0164799.

Naveena, B. B. K. A. S. 2011. IJPBS Article-Antitumor activity of *Aloe vera* against Ehrlich Ascitis Carcinoma (EAC) in Swiss albino mice. Available at: https://ijpbs.net/abstract.php?article=NzQy (Accessed: 15 August 2020).

Ortega-Toro, R., Sofía Collazo-Bigliardi. Josefa Roselló, Pilar Santa marina, Amparo Chiralt. 2017. Antifungal starch-based edible films containing *Aloe vera*, 72. November 2017: 1-10.

Parthasarathy, G., Saroja, M., and Venkatachalam, M. 2017 'Bio-synthesized nano-formulation of zinc oxide-*Aloe vera* and to study their characterization and antibacterial activities against multiple pathogens', *International Journal of Pharmaceutical Sciences and Research*, 8(2), pp. 900–907.

Paul, S., Somit D, Chaudhuri TK, Bhattacharjee K. 2014. 'Anti-inflammatory and protective properties of *Aloe vera* leaf crude gel in carrageenan induced acute inflammatory rat models', *Int J Pharm Pharm Sci*, 6(9), pp. 368–371.

Putri, G. A. and Medawati, A. 2016. 'Daya hambat ekstrak etanol *Aloe vera* L. terhadap proliferasi sel kanker rongga mulut (Sp-C1) secara *in vitro*', *Mutiara Medika: Jurnal Kedokteran dan Kesehatan*, 12(1), pp. 19–23.

Ramz, K., Abbasi N, Hafeziahmadi M, Azizi M, Hedayatpour A, Abbaszadeh H, Moayeri A. 2016. 'Effect of different concentrations of *Aloe vera* leave's extract on the healing process of rat's second degree burn', *Journal of Basic Research in Medical Sciences*, 3(4), pp. 34–39.

Rivandi, M., Emami MR., Rad M., Mehrjerdi HK., Azizzadeh M., and Ghasemi S. 2012. 'Bacteriological evaluation of *Aloe vera* L. fresh gel on experimental infected full-thickness open wounds induced with *Staphylococcus aureus* in dogs', *Iranian Journal of Veterinary Surgery*, 7(1–2), pp. 75–84.

Shireen, F., Manipal, S., and Prabu, D. 2015. 'Anti-fungal activity of *Aloe vera*: *In vitro* study', *SRM Journal of Research in Dental Sciences*, 6(2), p. 92.

Singh, B., Sharma V., Dhiman A and Devi M.. 2012. 'Design of *Aloe vera*-alginate Gastroretentive Drug Delivery System to improve the pharmacotherapy', *Polymer - Plastics Technology and Engineering*, 51(13), pp. 1303–1314.

Zandi, K., Zadeh MA., Sartavi K. and Rastian Z. 2007 'Antiviral activity of *Aloe vera* against herpes simplex virus type 2: An *in vitro* study', *African Journal of Biotechnology*, 6(15), pp. 1770–1773.