

A Detailed Study of Aloe Barbadensis Phytochemistry, Taxonomy and Its Anticancer Activity

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ABSTRACT

Aloe barbadensis Mill., the scientific name of which is *Aloe vera* plant, is an essential perennial succulent plant with tremendous medicinal and pharmacological values. This species falls under the family Asphodelaceae and possesses thick fleshy and lanceolate leaves which are basal and in a rosette structure, the inner parenchyma has gel and the pericyclic region contains yellow latex. For centuries, *Aloe barbadensis* has been incorporated in different cultures in ethnomedical practices whereby it is used for the management of burns, wound, skin infection and gastrointestinal problems. The plant contains bioactive attributes mainly because it has contained a variety of phytochemical constituents which include polysaccharides like acemannan and glucomannan, anthraquinones as aloin A, aloin B, emodin, chromones namely aloein, vitamins C, E, B complex, enzymes such as bradykinase and amylase, amino acids, and minerals and fatty acids. These constituents have a combined effect of biological functions such as antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory activities. Specifically, several scientific studies have revealed that *Aloe barbadensis* could have potential medicinally active anticancer properties based on its properties such as apoptosis, antiproliferation of tumor cells, oxidative stress, and angiogenesis. Alchemical compounds like aloin and emodin have exhibited good cytotoxicity to a number of cancer cell lines from breast, colon and liver cancer cells. It is also necessary to give the brief information about *Aloe barbadensis* including taxonomy, morphological differentiation of the plant from other *Aloe* species, phytochemistry and various other compounds, and the effectiveness of this plant as an anticancer agent.

Keywords- *Aloe barbadensis*, phytochemistry, taxonomy, Anticancer.

I. INTRODUCTION

Aloe vera (*Aloe barbadensis* Miller, family Xanthorrhoeaceae) is a perennial green herb with bright yellow tubular flowers that is extensively distributed in hot and dry areas of North Africa, the Middle East of

Asia, the Southern Mediterranean, and the Canary Islands. *Aloe vera* derives from “Allaeh” (Arabic word that means “shining bitter substances”) and “Vera” (Latin word that means “true”). The colorless mucilaginous gel from *Aloe vera* leaves has been extensively used with pharmacological and cosmetic

applications[1]. Traditionally, this medicinal plant has been employed to treat skin problems (burns, wounds, and anti-inflammatory processes). Moreover, *Aloe vera* has shown other therapeutic properties including anticancer, antioxidant, antidiabetic, and antihyperlipidemic. *Aloe vera* contains more than 75 different compounds, including vitamins (vitamin A, C, E, and B12), enzymes (i.e., amylase, catalase, and peroxidase), minerals (i.e., zinc, copper, selenium, and calcium), sugars (monosaccharides such as mannose-6-phosphate and polysaccharides such as glucomannans), anthraquinones (aloin and emodin), fatty acids (i.e., lupeol and campesterol), hormones (auxins and gibberellins), and others (i.e., salicylic acid, lignin, and saponins)[2].

II. HISTORICAL AND TRADITIONAL MEDICINAL USES OF ALOE BARBADENSIS

Aloe barbadensis Mill. or *Aloe vera* has a historical medicinal background that extends through countless millennia across many societies around the world. Throughout history *Aloe vera* established its status as a plant of healing through traditional medicinal practices that continue to find application in modern herbal medicine systems. The large number of documented uses for *A. barbadensis* can be found in classical as well as traditional medicine systems throughout the world[3].

2.1. Ancient Egyptian medicine

The people of ancient Egypt used *Aloe vera* plant since the time when it earned the title of “plant of immortality.” Cleopatra and Nefertiti among other Egyptian queens employed *Aloe gel* every day for their beauty routines and skincare. Egyptian society used *Aloe* in two distinct ways: first for cosmetic purposes and second to preserve bodies for burial as they placed the substance in tombs to signify eternal life. *Aloe vera* features across different remedies within the Ebers Papyrus medical document written during 1550 BCE for addressing skin infections together with ulcers and internal diseases[4].

2.2. Greek and Roman medicine

In Greek and Roman times, people have also used *Aloe vera* for the same purpose of treating wounds and swellings. In mustering every possible use of *Aloe* the Old World knew, Dioscorides mentioned that it can be used in sores, hair treatment, gonorrhea and hemorrhoids. Pliny the elder, a Roman naturalist also knew the plant to help treated oral and skin infection. Ewings Rome was one of the Roman soldiers who allegedly treated injuries and sunburn achieved using *Aloe* extracts during a battle.

2.3. Traditional uses

Aloe vera, or *Aloe barbadensis* Miller, has long been valued for its nutritional and therapeutic properties.

This chapter explores the various uses of *Aloe vera* for human health as well as its botanical characteristics and phytochemical composition. *Aloe vera* is a plant that produces a gel-like substance from its succulent leaves. It is rich in bioactive substances such as monosaccharides, enzymes, fatty acids, vitamins, minerals, and aloe-emodin. Its many therapeutic benefits, including wound healing, anti-inflammatory effects, antioxidant activity, neurological health, antineoplastic qualities, antibacterial activity, gastrointestinal health, pain relief, and hormone regulation, are supported by these elements[5]. *Aloe vera*’s effectiveness in enhancing skin health, immunological function, metabolic regulation, and hematological effects is supported by clinical research. *Aloe vera* also shows promise in reducing the negative impacts of environmental pollutants. Its high nutritional content is highlighted by its nutrient-rich composition, offering a spectrum of dietary benefits. *Aloe vera*’s adaptability and historical use mark its significance across cultures and its modern applications in cosmetics, health, and nutrition. By exploring its extensive medicinal and nutritional attributes, this chapter elucidates *Aloe vera*’s holistic role in promoting human well-being and its enduring legacy in traditional and contemporary healthcare practices[6].

III. TAXONOMY AND BOTANICAL DESCRIPTION

Aloe barbadensis Mill., commonly known as *Aloe vera* (L.) Burm.f, is one of the several types of the species of the *Aloe* category of plants, which is a genus of flowering succulence plants. It is in the family Asphodelaceae of the subfamily Asphodeloideae within the order Asparagales. This taxonomic classification has been changed in recent years because the morphological difference between species of *Aloe* has been very small and due to certain general tendency of keeping interspecific hybrids[7]. *Aloe barbadensis* mentioned in Fig.1.



Fig.1: *Aloe barbadensis*

Table 1: Taxonomic classification

Kingdom	Plantae
Clade	Angiosperms

Clade	Monocots
Order	Asparagales
Family	Asphodelaceae
Genus	Aloe
Species	<i>Aloe barbadensis</i> mill.

Botanical description

Aloe barbadensis Mill., that is Aloe vera, is astemless or short-stemmed plant which is also a xerophytic perennial succulent herb of the family Asphodelaceae. It is often grown in a rosette form with the height of 60-100 cm. It preferably grows in desert areas and shows some features of the xerophytic plant possessing vascular tissues and CAM for water storage[8].

They are arranged spirally in a ring round the stem and are broadly lanceolate, and fleshy measuring between 30-50 cm long and 6-7 cm broad at the base. They are develop in range from green to grey-green to a dreary green shade and possess waxy cuticle and juvenile gonococci typically manifest white spots. The edges of the leaf are serrated with white and sharp small spines with about 2-3 mm long[9]. Internally, each leaf has three distinguishable layers namely, the chlorenchyma or the outer skin, the second layer containing yellow latex which is bitter and consists of anthraquinones, and the inner layer consisting of mucilage which is mainly composed of polysaccharides enzymes, amino acids, vitamins and other trace elements.

3.1. Morphological characteristics

Aloe vera which shows stem-less or short stem plant habit; it is xerophytic perennial plant belongs to family, Aloeaceae. This plant grows to a height of about 60-100cm and grows well in arid conditions of the country. One of them is the thick and fleshy leaves which are spirally arranged in a basal rosette manner. They are narrowly lanceolate, acuminate with medium-textured blotches measuring between 30- 50 cm in length and 6-7 cm in width at its base. The colour ranges from green to grey green bearing pale white speckles on the young part of the leaves has a waxy and smooth epidermis. The margins are also blunt with small white or off white triangular spines about 2-3mm in length. On the internal layering, the common features of the leaf margins and terrain have three parts: cuticle Chlorenchyma, subcutaneous containing yellow latex anthraquinone compounds include aloin., and the last, oil filled parenchyma interior, a water, polysaccharides, amino acids and vitamins[10].

It has a terminal or axillary, panicle or racemose inflorescence that can grow up to 90 cm tallmass. The tubular flowers are pendulum or pendent and drooping or ovate, yellow to orange in color, 2 or 3 cm in length. Most of them can be said to be bisexual and commonly produced by insects. The plants possess fibrous root system which is spread out and not very

deep, consequently they are well adapted to take water from just below the surface of the soil. *A. barbadensis* is mostly reproduced asexually through division by vegetative means through offshoots, commonly referred to as 'pups' and, in very favorable circumstances, via seed production. Such morphological characteristics that help the plant to establish well in different ecological conditions and to find wide use in traditional and modern medicine[11].

3.2. Distribution and cultivation practices

Aloe barbadensis Mill., better known as *Aloe vera*, is estimated to originate from the Arabian Peninsula but at present is a native weed that is widely cultivated in tropical as well as subtropical regions. The plant's ability to grow in warm and dry areas enhances its spread in Africa, India, South and South Central USA, South-Eastern Asia, the Mediterranean, America, the Caribbean and some parts of California. The plant prefers and grows well on raised plantations, sandy to loamy soils and known to grow best in fully sunlight areas with little or little rainfall. It grows best at between 20 and 30 ° C and intolerance to frost as well as water logging[12].

Most often, cultivation is through vegetative means through the use of basal offshoots or suckers that provide each plant uniformity when growing as well as rapid growth as compared to seed propagation[13]. The plant is often planted 60 to 90 cm apart to ensure sufficient space for the formation of the leaves and an easily accessible canopy for purposes of a lay in harvesting. For the preparation of the soil some studies require raking and perhaps a light tilling to remove some weeds and inclusion of organic compost or farm yard manure for soil enhancement. Watering is done sparingly and only when the plants are drying up because too much moisture reduces the chances of root. Harvesting of mature leaves starts 8 to 12 months after planting and it is done by hand to avoid any harm to the plant leaves. For these reasons, *Aloe barbadensis* has highly potential for crop production and is a suitable crop to be produced in sustainable agricultural system and in dry land farming systems[14].

IV. PHYTOCHEMISTRY

Aloe barbadensis Mill, known as Aloe vera, is the globe's best-known species of Aloe plant due to its various uses in medicine and cosmetics. This makes it rich in phytochemicals and it is these agents which are responsible for its biological actions. Some of the other useful chemical compounds found in the plant are anthraquinones, chromones, polysaccharides, flavonoids, sterols, enzymes, amino acids, vitamins and minerals[15]. The carbohydrates are, primarily located in the two broad regions of the leaf; the outer green skin and the inner water-filled parenchyma or gel layer. The components of the mixture are different and have a

different chemical makeup along with different pharmacological properties.

The compounds present in the Aloe vera, particularly anthraquinones and derivatives of anthraquinones can be considered as most investigated within the present day. These are mainly situated in the yellow yellow latex ooze that forms within the layer of skin on the leaf. The chief anthraquinone glycoside is aloin which comprises of two interconvertible substances under the name of aloin A and aloin B otherwise known as barbaloin[16]. It seems that these compounds have very strong laxative properties due to their ability to stimulate peristaltic movements as well as to enhance the water content in the colon. After the hydrolysis the aloin is transformed to aloe-emodin that has proven to possess antimicrobial, anti-inflammatory and anticancer properties. Also, emodin and isobarbaloin are present in a comparatively lesser content with aloe-emodin.

Aloin and several chromones including aloesin and aloeresin A are the characteristic compounds which are found only in Aloe species. Among the Aloesin derivatives, special emphasis should be given to antioxidant, anti-inflammatory, and tyrosinase inhibition activities, which can be considered the compound as an object for dermatological use[17].

The inner gel of the plant is especially featured with polysaccharides, which are known to produce immunomodulating and therapeutic effects in case of skin injuries. The most abundant polysaccharide was identified as acemannan which is mannose polymer composed of (1 to 4) joint and contains some acetyl groups[18]. As stated earlier, Acemannan has been found to possess immunomodulatory effects on the macrophage, increase cytokine synthesis, and proliferation of tissue formation. Glucmannans, galactans and arabinans are other saccharides also contained in the gel that assist in offering the gel viscoelasticity and hydration properties Fig.2.

The phenolics are present in reasonable amounts and contribute mainly to the facilities antioxidant activity of Aloe vera. Some of the flavonoids which were found include kaempferol, quercetine, and their derivatives. These compounds found in the plant have Free travels, anti-inflammatory, and antibacterial properties thus improving the efficacy of this good plant[19].

Aloe vera contains various phytosterols among which campesterol, β -sitosterol, lupeol and stigmasterol are to be found mainly in the pulp of the leaf. These sterols possess anti-inflammatory and antidiabetic effects by regulating the markers of inflammation and glucose homeostasis. Of all those sterols found in the leaves of *Z. nigrum*, lupeol has attracted considerable attentiveness because of their anticancer and antimicrobial properties[20].

For example, the leaf gel has enzymes such as amylase, lipase, carboxypeptidase, and bradykininase for

inflammation and anti-inflammatory action as well as in digesting food. Bradykininase for instance has a role in counteracting pain and inflammation since it neutralizes bradykinin an inflammatory agent. It is noteworthy that the organic acids include malic acid, citric acid, succinic acid, which can also play a role in the preservation of a gel and energy metabolism[21-23].

The essential micronutrients exist in aloe vera plants. Aloe vera possesses beta-carotene and vitamins C and E together with unusual plant vitamins B1 (thiamine) B2 (riboflavin) B6 (pyridoxine) and B12. The antioxidant defenses of cells together with cellular metabolic processes gain support from these vitamins. *Aloe vera* provides numerous essential nutrients comprising calcium as well as magnesium and zinc and selenium together with iron and potassium which are vital for body operations[24].

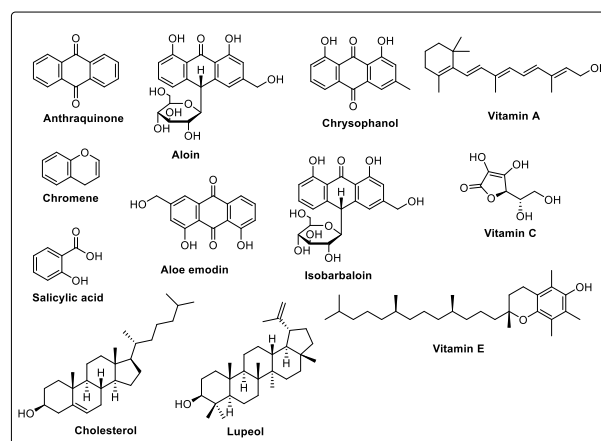


Fig.2: Phytochemical structures of *Aloe barbadensis*

V. IN VIVO AND IN VITRO EVIDENCE OF ANTICANCER EFFECTS OF ALOE BARBADENSIS

Tong et al.,2021 The primary objectives of this research were to investigate the anticancer effects of *Aloe barbadensis* extract C (AVBEC) in cell lines and to ascertain whether or not it is safe to administer to rats. The administration of AVBEC to Sprague-Dawley (SD) rats through oral administration was the means by which we established the safety of this compound. The first study focused on acute toxicity, while the second study investigated chronic toxicity over a period of six months. A further investigation was conducted to determine whether or not AVBEC was cytotoxic to both cancer cells and normal cells. At the same time as we were investigating the role of an AVBEC component, we continued our work into the anti-tumor action of AVBEC. Both the acute toxicity study, which required a dose of 44.8 g/kg^{-1} , and the chronic toxicity study, which was conducted over a period of six months and required a dose of 4.48 g/kg^{-1} , were unsuccessful in identifying

any substance-related toxicity or fatalities. In the chronic toxicity trial that included AVBEC, there was no evidence of organ toxicity, including impairments in chemical and structural function, or injury to the central or peripheral immune systems. This applies to both the central and peripheral immune systems. In addition, AVBEC was able to trigger cancer cell apoptosis with a significantly higher apoptotic ratio compared to non-cancer cells. This was accomplished by reducing the quantity of adenosine triphosphate (ATP) and boosting the formation of reactive oxygen species (ROS). Furthermore, we utilised high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) in order to identify components in AVBEC. This was done in addition to our investigation into the role that malic acid plays. While malic acid was able to induce cell necrosis in cancer cells as well as non-cancer cells when subjected to the same conditions, AVBEC did not have any similar impact[25].

Chen *et al.*,2004 The purpose of this study was to evaluate the chemopreventive action of aloe-emodin in human promyelocytic leukaemia HL-60 cells *in vitro*. This was accomplished by assessing the control of proliferation, cell cycle, and apoptosis. HL-60 cells were subjected to apoptosis, G2/M arrest, and suppression of cell proliferation as a result of the presence of aloe-emodin. When we used immunoblot analysis to examine the levels of cyclins B1, E, and A in HL-60 cells, we discovered that cyclin E remained unchanged, although the levels of cyclins B1 and A both increased. When looking at the levels of cyclin-dependent kinases (Cdks), aloe-emodin was shown to increase the levels of Cdk1 in HL-60 cells, but it had no effect on the levels of Cdk2. Increased levels of p27 were seen in HL-60 cells that were subjected to cotreatment with varying concentrations of aloe-emodin. Raising the levels of p27 is one of the potential mechanisms by which aloe-emodin triggers G2/M arrest in the cells that are the subject of this investigation. Additionally, experiments utilising DNA fragmentation gel electrophoresis and flow cytometrics demonstrated that aloe-emodin was responsible for the death of HL-60 cells. A significant increase in Caspases-3 levels was seen after 12 hours, 24 hours, 48 hours, and 72 hours of cotreatment of HL-60 cells with 10 µM aloe-emodin. Taking everything into consideration, it appears that aloe-emodin activates caspase-3 in human leukaemia HL-60 cells, which stops the proliferation of these cells and causes them to undergo cell cycle arrest and apoptosis, so demonstrating its ability to inhibit the development of cancer[26].

Chun xiao *et al.*,2008 In order to have a better understanding of the actions and processes that emodin performs in prostate cancer cells. It was evaluated by the use of the MTT assay whether or not the LNCaP and PC-3 cells that had been treated with emodin were viable. A agarose gel electrophoresis was used to analyse the DNA fragmentation that occurred after the emodin treatments were performed. Flow cytometric analysis

was utilised in order to obtain information on the expression of Fas and FasL, in addition to the apoptosis rate. For the purpose of determining the levels of androgen receptor (AR), prostate-specific antigen (PSA), p53, p21, Bcl-2, Bax, caspase-3, -8, -9, and Fas DNA expression, Western blotting was utilised. On the other hand, real-time polymerase chain reaction (RT-PCR) was utilised to evaluate the levels of expression of these proteins. Emodin, in contrast to PC-3, was able to cause a considerable reduction in the proliferation of LNCaP cells while simultaneously causing an increase in autophagy. It was observed that the expression of AR and PSA was decreased as the concentration of emodin increased, however the expression of p53 and p21 was increased. In addition, emodin led to an increase in the ratio of Bax to Bcl-2 and an upregulation of caspase-3 and -9, which ultimately resulted in the death of LNCaP cells. On the other hand, neither the Fas nor the caspase-8 proteins demonstrated any signs of being affected. The mitochondrial pathway is responsible for the death of cells caused by emodin, whereas the AR and p53-p21 pathways are responsible for the suppression of proliferation in the LNCaP prostate cancer cell line cells[27].

Zhang *et al.*,2017 Aloesin, which is a key component of aloe vera, possesses qualities that include antibacterial, anti-inflammatory, and UV-protective capabilities. Our goal is to get an understanding of the mechanisms by which aloesin contributes to the proliferation and metastasis of ovarian cancer cells, as well as any potential avenues by which it may do so. Both cell survival and cell clonality were inhibited by aloesin in a manner that appeared to be dose-dependent. In SKOV3 cells, it causes cell death by stopping the cell cycle in its S-phase, which results in cell death. Within the context of an *in vivo* study, it was discovered that aloesin inhibits the formation of tumours. Furthermore, it reduced the capacity of SKOV3 cells to migrate and decreased the likelihood that they would infiltrate other cancer cells. It is a fascinating discovery that the phosphorylation of members of the mitogen-activated protein kinase (MAPK) family decreased as the dosage of aloesin was increased. Therefore, it would appear that the MAPK signalling pathway is responsible for mediating the anticancer effects of aloesin[28].

Yonehara *et al.*,2015 There is a type of solid tumour that affects children called neuroblastoma, and it is resistant to the capacity of chemotherapy to remove it fully. In order to determine whether or not Aloe vera (AV), a potential anticancer reagent, could be beneficial in the treatment of neuroblastoma, we investigated the anti-proliferative effects of an extract of AV protein. Materials and Methods of Procedure: following being incubated with AV protein extract, the proliferation status of four distinct human neuroblastoma cell lines was determined. These cell lines were IMR-32, TGW, CHP-126, and NBL-S. Cell counting, Ki-67 staining, and gene expression were determined following the

incubation process. When compared to the untreated control group, the number of viable IMR-32 cells that were treated with AV experienced a significant decrease of 1.98 times by day 2 and 1.33 times by day 5 of culture. This was observed among the lines that were analysed, with a statistical significance of $p < 0.05$. Furthermore, by the fifth day, the therapy had resulted in a reduction of 13% ($p < 0.05$) in the frequency of Ki-67(+) IMR-32 cells. On the other hand, on day 1, the levels of CCND2 mRNA expression were no longer detectable, in contrast to the controls that had not been treated with any treatment. It has been determined that AV-protein extract is capable of inhibiting the growth of human IMR-32 neuroblastoma cells in vitro. This is most likely accomplished by reducing the levels of CCND2 mRNA[29].

Lee et al.,2006 In H460 cells, researchers noticed DNA aggregation when aloe-emodin caused cell death. The comet assay demonstrated that Aloe-emodin (40 μ M) induces single-strand breaks in DNA. The amounts of mRNA for DNA repair enzymes, including hMTH1, hOGG1, and APE, were observed to be decreased by aloe-emodin. The effects of aloe-emodin on H460 cell apoptosis were thought to stem from its prooxidant properties, despite the substance enhancing the activity of the radical-scavenging enzyme SOD. The findings suggest that aloe-emodin may induce DNA damage in human lung cancer cells through the generation of reactive oxygen species[30].

Majumder et al.,2020 *Aloe vera* leaves contain bioactive molecules that bind to the oestrogen receptor in a significantly more powerful manner than the well-known drug tamoxifen, which is considered to be the gold standard. The results of our research indicate that when compared to the IC₅₀ (332 μ g/mL) of *Aloe vera* leaf extract against a non-cancerous cell line (NIH-3T3), the IC₅₀ of the extract against a breast cancer cell line (MCF-7) is substantially lower, measuring at 23 μ g/mL. Finally, our findings revealed that the *Aloe vera* leaf extract had a total content of phenolic acid, which was found to be 385.662 μ g/mL, flavonoids, which were found to be 160.402 μ g/mL, and alkaloids, which were found to be 276.754 μ g/mL. The extract of aloe vera leaf exhibits a free radical scavenging activity that ranges from 67% to 89% when applied at doses ranging from 50 to 300 μ g/ml. In our virtual molecular docking investigation, we discovered that bioactive substances such as aloe-emodin (-8.8 Kcal/mol), 7-hydroxy-2,5 dimethylchromone (-7.5 Kcal/mol), beta-sitosterol (-7.3 Kcal/mol), and others bind to the oestrogen alpha receptor with a greater degree of strength than the conventional medicine tamoxifen (-6.4 Kcal/mol)[31].

Tseng et al.,2017 Through a variety of different regulatory pathways, aloe-emodin (AE), which is derived from the plant *Aloe vera* and the herb rhubarb, has been shown to have anticancer effects in a variety of different types of cancer. There is a lack of understanding regarding the effects that AE has on

anticancer medications such as cisplatin, doxorubicin, docetaxel, and 5-fluorouracil. Experiments on cell viability were carried out after the breast cancer cell lines MCF-7, MDA-MB-231, MDA-MB-468, BT-474, and HCC-1954 were subjected to the AE conditions that were defined. For the purpose of determining the levels of signalling protein expression, Western blotting, intracellular reactive oxygen species (ROS), cell cycle distributions, and flow cytometry were utilised. As a result of the reduction in EGFR, ER α , Ras, ERK, c-Myc, and mTOR protein expression, as well as the blocking of PI3K and mTOR activation, the cytotoxicity of 9 μ g/ml tamoxifen was enhanced by AE. This meant that MCF-7 cells were more susceptible to the effects of AE treatment compared to other cells. In conclusion, there were no effects on the advancement of the cell cycle; nevertheless, there was an increase in the amount of reactive oxygen species (ROS) that were produced inside the cells as a result of the co-treatment of AE and tamoxifen. As evidence of its chemosensitizing ability, AE did more than only aid in the death of cells that were triggered by tamoxifen; it also improved the antiproliferative activity of tamoxifen in breast cancer cells by suppressing the Ras/ERK and PI3K/mTOR pathways[32].

Liu et al.,2018 A novel photosensitizer (PS) named aloe emodin (AE) was subjected to photodynamic therapy (PDT) in order to inhibit human oral squamous cell carcinoma. The outcomes of this inquiry are presented here. The investigation was conducted in vitro and in vivo. AE-PDT was able to inhibit cell migration, and optical microscopy was able to identify unique morphological alterations in cancer KB cells that were found in the oral mucosa. During the G1 phase of cell growth, massive reactive oxygen species (ROS) were formed by photoactivated AE, which were responsible for stopping cell growth and increasing apoptosis independently. As a result of AE-PDT, it was discovered that the levels of Caspase-3 and Bax proteins were increased, whilst the levels of Bcl-2 protein were observed to be decreased. Although there were no adverse effects recorded, AE-PDT was able to dramatically slow the growth of tumours in mice following transplantation and increase the amount of time that cancer mice were able to survive. Evidence suggests that AE-mediated photodynamic treatment (PDT) is a unique strategy to treating oral cancer that maintains the integrity of the tissue while reducing invasion and does not have any adverse effects on the major organs[33].

Chen et al.,2016 With the purpose of gaining a better understanding of how aloe-emodin functions as a photosensitizer, the purpose of this study was to investigate the processes of photo-cytotoxicity that are generated by aloe-emodin in breast cancer MCF-7 cells. After being subjected to photodynamic treatment with a variety of aloe-emodin concentrations and light doses, the study of cell proliferation revealed a considerable

reduction. Apoptosis processes were found to be related with death pathways that involved the mitochondria and the endoplasmic reticulum, and we demonstrated that these variations in apoptosis were associated with these routes. The researchers were able to examine the adhesion, migration, and invasion skills of breast cells by using the WST8 and transwell assays. Additionally, they discovered that AE-PDT significantly reduced these capacities in MCF-7 cells. Oxidative stress was found to be related with the metastasis, as demonstrated by the production of matrix metalloproteinases 2, 9, VEGF, and Nrf2. After receiving AE-PDT therapy, the cytoskeleton was found to be in a state of disorder, as determined by an evaluation of changes in cytoskeleton components (F-actin). Taking everything into consideration, the findings presented here revealed that aloe-emodin photodynamic therapy (PDT) was able to successfully suppress the progression of cancer in MCF-7 cells. This suggests that AE may have the potential to act as a novel photosensitizer in PDT, which would open up new pathways for the treatment of cancer[34].

Yeh et al.,2003 One of the components of *Rheum palmatum*, known as aloe-emodin (1,8-dihydroxy-3-(hydroxymethyl)-anthraquinone, has been discovered to possess anticancer qualities. However, the precise mechanism by which these compounds exert their anticancer effects is still a mystery. Through the use of the H460 human lung nonsmall cell carcinoma cell line, we investigated the mechanism by which aloe-emodin induced cell death. In order to induce cell death in H460 cells, aloe-emodin, at a concentration of 40 μ M, alters the expression of multiple proteins. These proteins include cAMP-dependent protein kinase, protein kinase C, Bcl-2, caspase-3, and p38. The investigation of the mechanisms by which aloe-emodin regulates apoptotic cell death has prompted researchers to investigate the interaction between several cell death signals. These signals include cAMP-dependent protein kinase, protein kinase C, Bcl-2, caspase-3, and p38-like proteins. It was demonstrated by us that the expression of p38 has a substantial influence on the apoptotic death that is triggered by aloe-emodin[35].

VI. CHALLENGES AND FUTURE PROSPECTS

However, there are some issues some of them are as follows concerning the use of *Aloe barbadensis* Mill. in the pharmacopeial system and modern medicine, which has not allowed it to gain a firmer footing. The first of them concerns the gross deficits of standardization of cultivation, processing, and extraction techniques. Due to these, the varying growth conditions, harvest time, handling and preparation techniques impact on the concentration and bioavailability of the contained phytotherapy bioactive compounds and consequently topicality and repeatability of the remedies.

Another important concern is that most of the pharmacological effects reported are not backed by clinical trials, especially in terms of the anticancer properties of the substance. In order to determine the same, more extensive in vivo and in vitro investigations have also been reported which is the need for extensive clinical trials to determine the safe therapeutic dose, possible drug combination, and safety profile of certain *Aloe barbadensis*-derived nucleotides and polysaccharides in the larger human population. In addition, some constituents like anthraquinones may pose certain problems since they caused cytotoxic and genotoxic effects in high doses or long-term usage, and therefore, the constituents should be stringently evaluated by toxicologists and regulatory authorities.

Furthermore, the extraction of compounds with biological activity out of complex plant matrices still poses a challenge to the researchers. These properties make it necessary to utilize higher-order analytic methodology and bioinformatics for more detailed examination of the effects of the isolated compounds and their combinations. However, the commercialisation of products based on *Aloe barbadensis* has continued to have challenges of regulatory and intellectual properties such as quality control standards safety for some of the products and compliance to the international standards.

Considering the future working prospects, the perspectives of *Aloe barbadensis* study are rather favorable. The improvements could be achieved by means of conventional and novel techniques like metabolic engineering, tissue cultures and genetic modifications to desired phytochemicals. Nanotechnology may enhance bioavailability and selective drug delivery in Aloe-based therapeutics due to their advanced characteristics. Therefore, further research in the other fields such as phytochemistry, molecular pharmacology, clinical medicine and even nanomedicine can enhance the discovery and development of other therapeutic compounds from *Aloe barbadensis*. Through the advancement in science and technology, this medicinal plant with natural remedy dates back in the past have a bright future towards embracing natural medicine.

VII. CONCLUSION

Aloe barbadensis Miller, commonly called *Aloe vera* is undoubtedly one of the most valuable scientifically and commercially explored medicinal plants in not only the traditional but the modern systems of medicine as well. The roots of this plant's use can be traced back to prehistory populations and, for this reason, its topical application represents a safe treatment for a wide array of conditions regarding the skin, inflammation and the gastrointestinal system. Originally members of Asphodelaceae family, the most noted taxonomic characteristics of *Aloe barbadensis* include succulence, rosette growth pattern, fundamental

adaptations that qualify the plant for xerophytic survival. This is because *Aloe barbadensis* contains phytochemicals; a factor that contributes to the plant's therapeutic uses. The plant has numerous bioactive compounds including polysaccharides include aecannan and glucomannan, anthraquinone includes aloin A, aloin B, and emodin exists in chromone and include aloesin, enzyme vitamins, amino acids, mineral and fatty acids. Most of these phytoconstituents can be found between the mucilage gel layer and the yellow latex of the leaf and are therefore accountable for the numerous pharmacological effects of the plant documented in literature as antioxidant, anti-inflammatory, antimicrobial, immunomodulatory, and wound healing properties of special focus in the current years has been the determination of possible antitumor effects associated with *Aloe barbadensis*. Experimental evidence indicate that one of its major compounds namely aloin and emodin, has some cytotoxic activity that triggers apoptosis, suppresses cancer cell proliferation, and influences oxidation and formation of blood vessels. The results of this study give a positive indications of the potential use of this plant in cancer chemoprevention and adjuvant treatment. Therefore, even though extensive in vitro and in vivo evidences were found showing its efficiency in cancer management, thus there is dire need for extensive clinical trials on human beings to determine the efficiency, safety, and pharmacokinetics of *Aloe barbadensis*-derived compounds.

In conclusion, it can be stated that there is a prospect for utilizing *Aloe barbadensis* in pharmaceutical industries due to its high pharmacological activity. Based on its revealed phytochemical composition and anti cancer activities it can be deemed as one of the most effective drugs in the future. Many tumorous structures which are considered as potentially antineoplastic compounds today have been detected in Iris, pharmacological and molecular investigation, as well as, clinical study of this plant demands for integration of interrelated sciences such as phytochemistry, pharmacology, molecular biology and clinical science in further research protocols.

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