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Synergistic Anticancer Potential Of Ginger, Bloodroot, And Aloevera: Development And Mechanistic Evaluation Of A Polyherbal Formulation

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Abstract: The present study focuses on the optimization and standardization of a polyherbal anticancer tablet formulation using three medicinal plants: Aloe vera, Bloodroot, and Ginger, selected for their known anticancer properties. Phytochemical analysis revealed the presence of flavonoids, alkaloids, phytosterols, and phenolic compounds in the plant extracts. The physical properties of the tablet granules, including angle of repose, bulk density, Hausner ratio, and compressibility index, indicated good flow characteristics. Tablets demonstrated uniformity in weight, adequate hardness, mechanical stability, and appropriate disintegration times within pharmacopoeial limits. Stability studies over three months showed no significant deviations in key parameters, confirming the formulation's stability. Acute toxicity tests, conducted in line with WHO and OECD guidelines, indicated high LD50 values, affirming the safety of the plant extracts. The in vivo anticancer activity was tested at concentrations of 200 and 400 mg/kg, with histopathological studies revealing the effect on solid tumors in various tissues. The polyherbal tablet formulation, developed on a laboratory scale, shows promise as a stable, cost- effective dosage form for potential use in cancer management, combining traditional medicinal knowledge with modern pharmaceutical techniques.

Keywords: Bloodroot, Aloe vera, Ginger, Polyherbal

I. INTRODUCTION

Plants have a unique position in the universe since they are the foundation of all life on Earth. They are the main producers in every food chain. Humans get 80% of their protein and 90% of their calories directly from plants. People have used plants as potential sources of medicine since the dawn of humanity. India is the source of the abundance of medicinal herbs, however traditional medicine is still practiced there. Therefore, it is imperative that this enormous natural resource be improved and used in accordance with the needs of humans and the growth of technology.

Cancer is one of the primary human diseases that causes huge suffering and economic loss world-wide. Chemotherapy is among the cancer treatments available. Unfortunately, the side effects of chemotherapy medications can be fatal and they are poisonous. New methods in the fight against cancer and its treatment in humans are constantly in the works. Natural ingredients provide the basis for around 60% of the anticancer

drugs currently available. A large number of currently used medications have natural products as their primary ingredient. Certain plants and herbal items include phytochemicals that may be used as therapeutic or preventative agents against different types of cancer in humans. The cell either gets rid of or stores the byproducts of the metabolic process when it absorbs chemical carcinogens. The cellular metabolism of carcinogens and their byproducts can influence the expression and functioning of genes in a variety of ways, including cell cycle control, DNA repair, development of cells, and cell death. A number of genotoxic processes, including chromosomal cracking, fusion, deletion, mis-segregation, and non-disjunction, are induced by some carcinogens. Iron, arsenic, and cadmium ions or molecules can cause chromosomal variations in quantity and structure. Some of these agents suppress the immune system, while others trigger inflammation, activate receptors like arylhydrocarbon or oestrogen receptors, generate reactive oxygen species, or even silence epigenetic factors. Hypermutability, a genome-wide loss of control over proliferation, immunity to apoptosis, and other hallmark traits of cancer cells may occur as a result of alterations to signal-transduction processes brought about by a mix of genotoxic and nongenotoxic causes.

II.PLANT PROFILE

1.ALOEVERA

Synonym: Aloe vulgairis Lamarek, or Aloe barbadensis Mil. or Aloe officinalis Forskal.

Botanical Classification:

- **Kingdom**: Plantae
- **Division**: Angiosperms
- **Class**: Monocots
- **Order**: Asparagales
- **Family**: Asphodelaceae
- **Genus**: Aloe
- **Species**: Aloe vera

Biological Source

Dried juice extracted from the undersides of the leaves of several varieties of Aloe plants is known as aloe vera. Members of the family Liliaceae, including Aloe perryi Miller, Aloe vera Linn, Aloe barbadensis Mil, and Aloe ferox Miller.

Geographical Source

Native to the Arabian Peninsula, Aloe vera is now widely cultivated in tropical, subtropical, and arid regions across the world. Countries like India, China, Mexico, the United States, and parts of Africa are notable for Aloe vera cultivation.

Plant Description

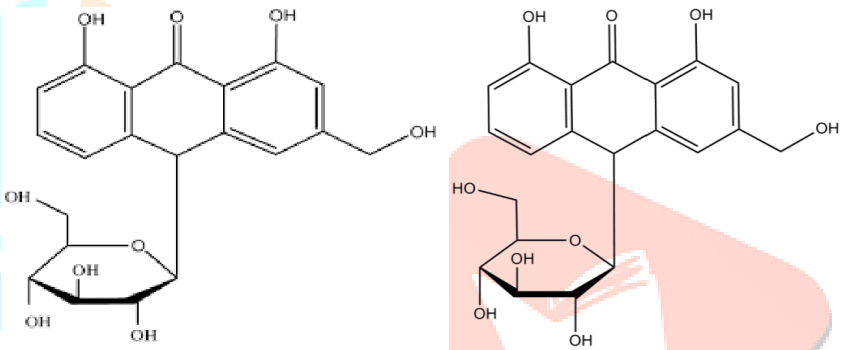
- **Type**: Perennial, succulent.
- **Size**: Typically grows 60–100 cm (24–39 inches) in height.
- **Leaves**:
  - Fleshy, thick, lance-shaped.
  - Greenish or gray-green with serrated edges.
  - Can grow up to 60 cm long and 8 cm wide at the base.

- **Flowers**:
  - Yellow or orange, tubular in shape, occurring in a spike up to 90 cm tall.
  - Blooms during the summer.
- **Roots**: Shallow, fibrous root system.
- **Stem**: Short, sometimes nearly stemless.

Chemical Constituents

The three key components of aloes, namely β-barboloin, are aloin isomers, Isobarbaloin, and Barbaloin. These three isomers form what is known as "crystalline" aloin and are to varying degrees (10% to 30%) throughout the course of treatment. Additionally, there are components such as resin, emodin, Aloe-emodin, and amorphous aloin. All of the cultivars include barbaloin, a crystalline glycoside that has a somewhat yellow color, is bitter, and is soluble in water. Crystalline isobarbaloin is found in aloe from Curacao, in trace amounts in aloe from Cape Cod, and missing from aloe from Socotrine and Zanzibar. β- and Barbaloin are the main ingredients of Zanzibar aloe and Socotrine.

2.GINGER



Synonyms

Rhizoma zingiberis, Zingibere.

Biological Source

The dehydrated rhizomes of the Zingiber officinale Roscoe plant, which is a member of the Zingiberaceae family, are what make ginger.

Origin and distribution

Africa, Nigeria, Jamaica, India, Japan, and the West Indies are the primary places where it is grown. Southeast Asian maritime regions are the source of ginger. It does not exist in the wild; it is a real cultigen. The earliest known evidence of its domestication dates back to the Austronesian peoples, who have long farmed and used several types of ginger. Other varieties of ginger were grown by them, such as bitter ginger (Zingiber zerumbet), white turmeric (Curcuma zedoaria), and turmeric (Curcuma longa). The leaves and rhizomes were either eaten raw or used to flavor dishes. Mats were also woven from the leaves. Aside from these applications, Austronesians considered ginger to be sacred, using it in healing rituals and in prayers to spirits for protection.

Characteristics

The rhizomes measure roughly 1.5 cm in thickness, 3 to 6 cm in width, and 5 to 15 cm in length. Branches of the Jamaica ginger are found. Its outer surface is buff yellow in color with longitudinally striated fibers, and it displays sympodial branching. The section of the buds has small circular depressions, and the broken surface displays a well-developed endodermis, a wide stele, and a slender bark with sporadic little points of fibrovascular bundles and yellowish secretion cell points. The ginger tastes strong and pleasant and has a fragrant, pleasant smell.

Chemical Constituents

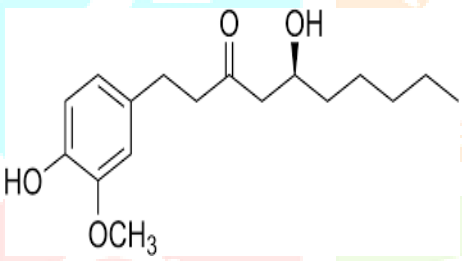
The distinct aroma and taste of ginger stem from its volatile oils, which make up 1-3 percent of the weight of fresh ginger. These oils are mainly composed of sesquiterpenes, which include zingerone, beta-bisabolene, zingiberene, shogaols, and gingerols. The main aromatic compound in ginger is -gingerol (1- [4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone). The chemical composition of raw ginger is about 400.

During the drying process, gingerols yield gingerone, which has a spicy-sweet scent and less pungency. Shogaols, which are more aromatic, are made from gingerols by heating, storing, or by acidity. Other components include a variety of compounds with monoterpenes, as well as amino acids, protein, fibre, phytosterols, vitamins, and minerals. Additionally, fresh ginger contains zingibain, an enzyme that catalyses cysteine proteases similar to rennet.

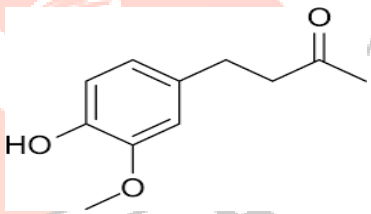
Ginger comprises starch, 5–8% pungent resinous substance, and 1–2% volatile oil. The medicine's pleasant perfume comes from the volatile oil, and its strong flavour comes from the odourless, yellowish-oily gingerol. Sesquiterpene hydrocarbons such as α-zingiberol, α-bisabolene, α-farnesene, and α-sesquiphellandrene, as well as α-sesquiterpene alcohol, make up volatile oil.

Some ingredients, such as shogaol and gingerone, are less strong. Fresh rhizomes do not contain shogal, which is a byproduct of gingerol's dehydration.

Gingerol



Zingerone



3.BLOODROOT

Synonym: Bloodroot; Bloodworth, Red Root, Red Puccoon

Biological Source

The poppy family Papaveraceae counts this plant as the sole member of the genus Sanguinaria.

Geographical Source

This wildflowers, which blooms in the spring, is native to North America and can be originate in verdant meadows from Nova Scotia and Florida westward to Nebraska, Manitoba, and Alabama. The permanent herbaceous flowering plant called bloodroot originates in the eastern part of North America. From the Atlantic coast to the Gulf of Mexico and beyond, westward to the Great Lakes and the Mississippi River embayment, bloodroot can be located throughout eastern North America.

Cultivation

Sanguinaria canadensis is grown for its aesthetic qualities. Gardeners appreciate the huge, brilliant white flowers that the double-flowered varieties produce quite early in the gardening season. Bloodroot flowers have a brief blooming show since their petals shed within a day or two of fertilization, while their double versions bloom for much longer. Because the stamens in the double blooms have been transformed into components resembling petals, pollination is more challenging.

Characteristics

The height of bloodroot ranges from 20 to 50 cm (8 to 20 in). It has one enormous basal leaf with five to seven lobes that can reach a diameter of up to 25 cm (10 in). Bright orange to crimson sap shoots from a reddish rhizome from which the leaves and flowers emerge. The genus name *Sanguinaria* (from the Latin *sanguinarius*, "bloody") derives from the color of the sap. Every year, the rhizomes lengthen and divide into colonies. In early spring, plants begin to bloom before the foliage appears. The leaves unfold to their full size following blossoming. Mid- to late-summer is when plants go dormant, It happens later than other fleeting spring flowers.

Chemical Constituents

When cut, bloodroot releases a brilliant orange-red sap from all parts of the plant; the rhizome, which stores the juices, has the largest concentrations. The sap is rich in starch, scarlet resin, and isoquinoline alkaloids. The phytochemicals. Isoquinoline alkaloids, primarily sanguinarine and chelerythrine, are abundant in sanguinaria root. Unlike most other alkaloids, sanguinarine, a benzophenanthridine alkaloid, exhibits a red color in aqueous solutions.

Isoquinoline alkaloids, primarily sanguinarine and chelerythrine, are abundant in sanguinaria root. Unlike most other alkaloids, sanguinarine, a benzophenanthridine alkaloid, exhibits a red color in aqueous solutions. The rhizomes and roots contain the highest and second-highest concentrations of it, respectively, with lower concentrations found in leaves and flowers. Protopine and berberine are two related chemicals found in the plant, along with other minor alkaloids.

III. Preparation of crude drug for extraction

The extract was made from certain plant leaves. Gathered and left to dry in the shade were specific plant leaves. The leaves were dried and then finely ground in a machine grinder. Then, sieve No. 16 was used to screen this coarse powder made from the leaves of various chosen plants. Additionally, they were kept for the extraction in an airtight container after passage.

To extract the desired elements from the unrefined drug, Soxhlet extraction is utilized.

A. Aloevera

Water was used as the solvent throughout the 48-hour extraction of 50 grams of dried coarse powder from Aloevera utilizing a Soxhlet equipment. After complete extraction, the aqueous extract was concentrated in a vacuum dryer at 40ºC under reduced pressure to preserve it in desiccators.

B. Bloodroot

50 grams of dried coarse Bloodroot powder were continuously extracted with water as the solvent for 48 hours using a Soxhlet device. After complete extraction, the aqueous extract was concentrated in a vacuum dryer at 40ºC under reduced pressure to preserve it in desiccators.

C. Ginger

Water was used as the solvent in a Soxhlet device to continuously extract 50 grams of dried coarse powder gingerwa over the course of 48 hours. Desiccators were used to store the dried extract that was created by concentrating the solution of water under less pressure at 40ºC in a vacuum drier after extracting.

IV. Result and Discussion

4.1 Morphology and Specifications of Aloe vera, Bloodroot, Ginger

The morphology study of **Aloe vera**, **Bloodroot** (Sanguinaria canadensis), and **Ginger** (Zingiber officinale) focuses on the physical characteristics and structure of these medicinal plants. Such studies provide important insights into their identification, growth patterns, and potential therapeutic applications. The examination of morphology includes the evaluation of external structures such as leaves, stems, roots, and flowers, helping in the characterization of each plant species.

Table No. 4.1: Morphology and physicochemical specifications of Aloe vera

Sr.No.	TEST	SPECIFICATION
1.	Colour	Powder Green in colour
2.	Taste	Bitter and Sweet
3.	Foreign Organic Matters	Nil
4.	Ethanol Soluble extractive	0.6%
5.	Water Soluble extractive	90 %
6.	Loss on Drying(Moisture content)	15 %
7.	Total Ash	5.4 %
8.	Acid insoluble ash	0.03 %

Table No. 4.2: Morphology and physicochemical specifications of Bloodroot

Sr. No.	TEST	SPECIFICATION
1.	Colour of dry powder	Reddish-orange in colour
2.	Taste	bitter
3.	Foreign Organic Matters	Nil
4.	Ethanol Soluble extractive	10.24%
5.	Water Soluble extractive	22.50 %
6.	Loss on Drying(Moisture content)	2.1%
7.	Total Ash	6.0%
8.	Acid insoluble ash	0.25%

Table No. 4.3: Morphology and physicochemical specifications of Ginger seed

Sr. No.	TEST	SPECIFICATION
1.	Colour	dark yellow or light brown to pale buff
2.	Taste	spicy
3.	Foreign Organic Matters	Nil
4.	Ethanol Soluble extractive	14.66%
5.	Water Soluble extractive	5.25%

6.	Loss on Drying (Moisture content)	1.8%
7.	Total Ash	12.26%
8.	Acid insoluble ash	0.5%

1.1 Extraction

Extraction of three plants were prepared individually as well as in combinations of 2:1:1 and 4:1:1 by continuous hot extraction using Soxhlet extraction method for 48 hrs. Physical examination was performed on the extracts (color, consistency).

Figure No. 5.1: Soxhlet Extraction of Aloevera

Figure No. 5.2: Soxhlet Extraction of Ginger

1) Considerations for the preformulation of plant extract tablet powder mixtures

Parameters	Angle of repose	Bulk Density (g/cm^3)	Tapped Bulk Density (g/cm^3)	Hausner Ratio	Compressibility Index (%)	Loss on Drying (%)
F1	27.12±1.13	0.783±0.015	0.901±0.021	1.15±0.029	13.04±2.23	0.982±0.003
F2	29.12±1.14	0.787±0.012	0.906±0.025	1.151±0.024	13.12±1.83	0.986±0.005
F3	25.51±1.70	0.775±0.012	0.898±0.016	1.159±0.031	13.67±2.35	0.983±0.002
F4	27.02±1.01	0.756±0.020	0.883±0.037	1.17±0.035	14.36±2.63	0.981±0.004
F5	30.87±1.58	0.779±0.019	0.909±0.029	1.167±0.014	14.29±1.03	0.980±0.003
F6	26.85±1.01	0.769±0.010	0.896±0.026	1.164±0.031	14.10±2.33	0.983±0.001

2) Evaluation parameters of tablets of Plant extract

Batch	Color	Odor	Texture	Hardness (kg/cm^3)	Friability (%)	Weight variation (mg)	Disintegration Test (min)
F1	Light Brown	Chracteristics	Smooth	7.05±0.123	0.98±0.142	499.01±0.71	5.09±0.80
F2	**Light**	**Chracteristics**	**Smooth**	**5.8 ± 0.15**	**0.62 ± 0.37**	**500.45±0.68**	**4.31 ± 0.26**
	Brown						
F3	Light Brown	Chracteristics	Smooth	6.99±0.159	0.99±0.159	500.49±0.85	5.12±0.65
F4	Light Brown	Chracteristics	Smooth	7.02±0.148	0.83±0.148	500.79±0.77	6.54±0.75
F5	Light Brown	Chracteristics	Smooth	6.94±0.154	0.94±0.154	500.50±0.75	4.00±0.5
F6	Light Brown	Chracteristics	Smooth	7.01±0.146	0.71±0.146	500.60±0.62	6.44±0.66

3) Analysis of the prepared tablet's impact on blood-related metrics

Treatment	Hematological parameters				
	Hb g (%)	**RBC (10^3 cells /mm^3)**	**WBC (10^3 cells/mm^3)**	**Platelets (10^5 cells /cu.mm)**	**PCV%**
Normal control	13.40± 0.12	4.82± 0.06	7.90± 0.10	2.58± 0.21	25.32±0.13
Cancer control	6.66± 0.04^{a**}	2.10± 0.15 ^{a**}	15.70±1.10 a**	1.64±0.15 ^{a**}	54.45±0.58 ^{a**}
DAL+5 flourouracil	12.60±0.18^{b**}	4.52±0.17 ^{b**}	10.70±0.10 b**	2.78±0.14 ^{b**}	29.37±0.28^{b**}
Treatment control 200mg.kg^{-1}	9.22±1.48 ^{b**}	3.15±0.15 ^{b**}	11.30±0.40 b**	2.11±0.13 ^{b**}	45.23±0.18^{b**}
Treatment control 400mg.kg^{-1}	10.80±1.16^{b**}	3.90±0.18 ^{b**}	11.80±0.20 b**	2.55±0.24 ^{b**}	36.70±0.22^{b**}

4) The prepared tablet's impact on the parameters that were derived

Treatment	**ILS %**	**CCC ml x 10^6**	**IBW grams**
Normal control	≥30 days	-	1.22±0.06
Cancer control	40%	1.76±0.18^{a**}	8.46±1.80^{a**}
5-flourouracil	90%	0.86±0.24^{b**}	1.69±0.06^{b**}
Treatment group 200mg.kg^{-1}	75%	1.34±0.12^{b**}	2.86±0.22^{b**}
Treatment group 400mg.kg^{-1}	78%	0.98±0.20^{b**}	2.24±0.11^{b**}

Conclusion

The Global Effects of Cancer and Complementary Medicine's Role

With its increasing incidence and fatality rates, cancer continues to rank among the world's most pressing health concerns. This has led to a rise in interest in complementary medicine, which emphasizes the use of herbal remedies in addition to traditional therapy. The possible anticancer benefits of polyherbal preparations,

which combine many medicinal herbs, have drawn attention among these alternative medicines. Because these formulations have therapeutic uses in conventional medical systems, they are widely employed.

Developing a polyherbal tablet product is the primary objective of this research with an anticancer focus. In order to guarantee effectiveness, safety, and stability, the main objectives are to improve the formula and standardize its preparation. Research in this study looks into the potential anti-cancer properties of the selected plants and the stability of the formulation as it is turned into a solid dosage form (tablet).

The following three medicinal plants were selected for assessment of their anticancer potential after a thorough analysis of the literature:

1. Aloe vera (Aloe barbadensis miller)
2. Bloodroot (Sanguinaria canadensis)
3. Ginger (Zingiber officinale)

These plants were chosen because they are already in use in medical settings and because they may have anticancer properties. Bioactive substances found in all plants, including phytosterols, alkaloids, flavonoids, and phenolic compounds, possess numerous demonstrated therapeutic applications, such as the ability to fight cancer and act as antioxidants.

- Aloe vera: Aloe vera includes chemicals that are known to have therapeutic qualities like aloesin and aloesin derivatives, which have shown anticancer and antioxidant effects.
- Bloodroot: This plant contains alkaloids, particularly sanguinarine, which looked into because of its capacity to cause cancer cells to undergo apoptosis, often known as the programmed death of cells.
- Ginger: Ginger contains chemicals such as gingerol and shogaol, which have anti-inflammatory and antioxidant activities, which are thought to help in inhibiting cancer cell proliferation and promoting cell death in tumors.

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