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Formulation and evaluation of herbal capsule based on Indian medicinal plants for cancer therapy

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Abstract
Aim: Formulation and Evaluation of Herbal Capsule Based on Indian Medicinal Plants for Cancer Therapy.
Objective: The study is carried to the perform brief description about cancer, medicinal plants and cancer drugs that have anticancer activity.
Study reviewed of cancer, anticancer drugs and anticancer medicinal plants *like* of cancer treatment.
Materials and Methods: The crude drug used are *Fagonia arabica, Phyllanthus niruri, Smilax china, swertia chirayita, Sphaeranthus indicus Enicostemma littorale* are collected and the powdered form of these drugs was prepared.
Results and Discussion: The *in vitro* MTT assay on MCF-7 breast cancer cell lines was carried out. MTT assay on MCF-7 breast cancer cell lines indicated that polyherbal capsule formulation exhibited enhanced cytotoxic effects at IC50 values.
Conclusion: At the different doses (10 to 100 µg/ml) of Sample A carried out for anticancer activity against MCF-7 cell line, the compounds Sample A showed good activity against breast cancer cell line when you compared to standard drug 5 FU.

Keywords: *Fagonia arabica, Phyllanthus niruri, Smilax china* swertia chirayita, *Sphaeranthus indicus, Enicostemma littorale*

Introduction
Cancer is a major public health burden in both developed and developing countries. It is an abnormal growth of cells in body that can lead to death [1]. Cancer cells usually invade and destroy normal cells. The These cells are born due to imbalance in the body and by correcting this imbalance, the cancer may be treated.
In Cancers are a group of diseases characterized by their ability to function. If the spread of cancer cells this stage is known as metastasis is not controlled, it can result in death. Cancer is caused by Population Measures and Cancer Incidence and many external factors (tobacco, chemicals, radiation and infectious organisms) as well as some internal (inherited mutations, hormones, immune conditions and random mutations) [2, 3].
Cancer: Excessive cell proliferation that has the potential to spread to other body areas, cancer is an illness caused by genetic or epigenetic changes in the somatic cells. They comprise a subgroup of cancer. The unchecked proliferation of cells known as neoplasms or tumors, which can be dispersed widely and form a lump or bulk [4, 5].
Chemotherapy involves employing traditional anticancer medications to treat recurrent malignancies throughout the body, yet these drugs have substantial adverse effects [6]. High dosages, non-specific distribution, extreme toxicity to healthy cells, insufficient medication concentrations at tumors or malignant cells, and the emergence of multidrug resistance are the main causes of adverse effects [19, 21]. Thus, ongoing research is being done to develop better anti-cancer treatments that can target tumor cells specifically while having the fewest negative effects on healthy tissues [7, 23].
One type of treatment called chemotherapy employs medications to target cancer cells. It is referred to as a "systemic treatment" because the medication enters the bloodstream, moves throughout the body, and destroys cancer cells where they are found [18]. Most of the time, the goal of the medications is to eradicate cancer cells from the body, regardless of where they may be located. However, this is not always the case. Since normal actively dividing cells in the gastrointestinal tract, reproductive system, and bone marrow are also affected by

chemotherapy. And most individuals have some degree of side effects in the hair follicles, such as nausea, vomiting, hair loss, mouth sores, and ulcers [8, 9].

Importance of developing novel anticancer formulations

1. Herbal medicines have been widely used around the world since at the ancient times. The use of 'herbs' in the treatment of various diseases with fewer side effects has significantly increased [10].
2. Phytoconstituents are the plant constituents used in herbal medicines which are responsible for the biological action.
3. Phytoconstituents are also required for standardization of herbal molecules. It depends on the age of the plant, time of collection, environmental condition, etc.
4. Various classes of phytoconstituents that are alkaloids, flavonoids, tannins, essential oils, etc.
5. These phytoconstituents are water-soluble but are big molecules and hence not able to cross that are the lipid membrane and thus are show poor absorption [11].
6. Limitations of using natural products as medicines are stability, absorption and therapeutic effects which can be overcome by Novel Drug Delivery Systems.
7. Nanomedicine involves utilization of the Nanotechnology for the human health welfare [12].

Growing interest in herbal remedies for cancer treatment

The main reasons for using herbal remedies than synthetic treatment are.

1. There will be less side effects when compared to synthetic treatment.
2. The impact of dose variation will be less.
3. The cost of herbal products will be economically less.
4. These will be the widely available.
5. They are easily biodegradable.
6. There will be no tedious steps in synthesis of herbal products.
7. The synthetic treatment may or may not cure completely.

Herbal treatment for cancer avoids various physical side effects like pain, nausea, vomiting, fatigue, anaemia, lymphedema, fertility problems and ostomies caused by different cancer treatments like chemo therapy, radiation therapy etc. which are synthetic treatments [13, 14].

Objectives

The study is carried to the perform brief description about cancer, medicinal plants and cancer drugs that have anticancer activity. Study reviewed of cancer, anticancer drugs and anticancer medicinal plants like *Fagonia arabica*, *Phyllanthus niruri*, *Smilax china*, swertia chirayita, *Sphaeranthus indicus* *Enicostemma littorale* of cancer treatment [15].

Materials and Methods

Martials

The crude drug used are chirata, Bhumi amla, chopchini, Gulmundi, Chirata Nepali are collected and the powdered form of these drugs was prepared.

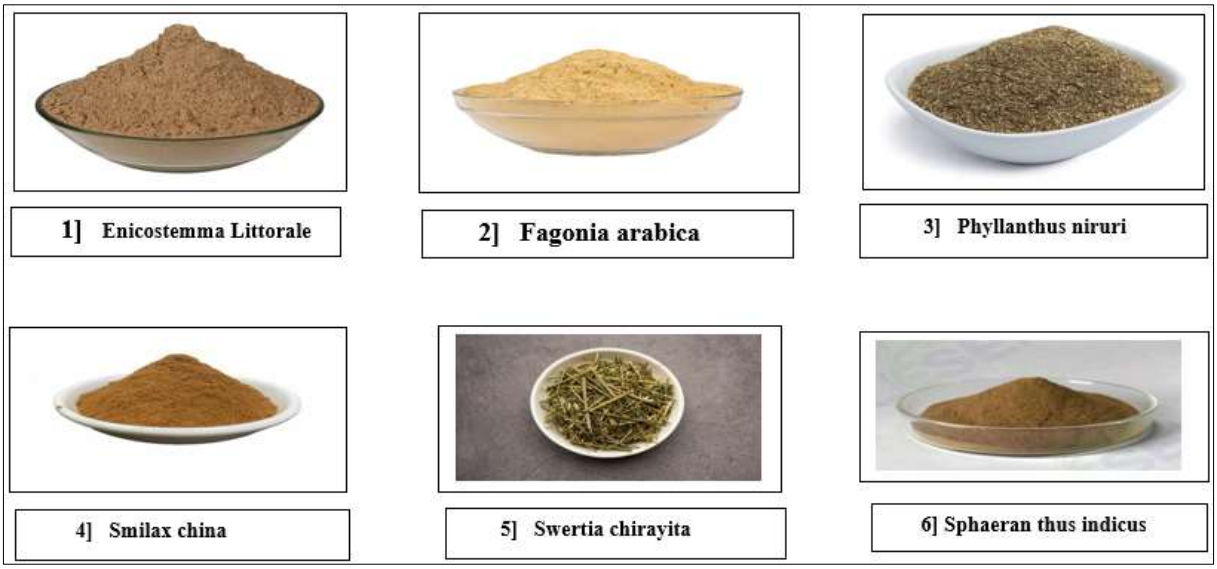

Fig 1: Selected crude drug for polyherbal formulation having potential anti-cancer activity

***In-vitro* screening of Formuation for breast cancer therapy**

***In vitro* cytotoxicity assay**

The inhibitory effect of individual extracts of C. longa, M. chamo-milla, W. somnifera and double and triple combination of extracts and their phytosomes were evaluated at different concentrations (10–100 mg/mL) at 24 h on MCF-7 cells and MDA MB 231 cell lines by adopting MTT assay. MTT assay on MDA MB 231 cell lines showed that the developed phytosomes showed minimal IC50 val- ues such as 40, 44, 42, 46, 42, 43, and 32 mg/mL in comparison to values of C. longa, M. chamomilla, W. somnifera, double and triple combination extracts (75, 80, 74, 57, 62, 55 and 46 mg/mL respetively). The assay determines the integrity of mitochondria andreflects the viability or otherwise of the cells. It was recorded that in a dose-dependent manner the extracts and phytosomes brought about cytotoxicity against the MCF-7 cell line

Procedure

All the required powdered mixtures were precisely weighted, and were passed through a standard sieve (sieve no 80) and blended for 5 and weight of all powder in 3 gm then all powder are mix and then fill the herbal capsule were prepared by compression method using single punch at the press machine.

Table 1: Formulation of herbal capsule

Sr. No.	Ingredients used	Quantity taken
1.	*Fagonia arabica*	3 gm
2.	*Phyllanthus niruri*	3 gm
3.	Smilax china	3 gm
4.	Swertia chirayita	3 gm
5.	Sphaeranthus indicus	3 gm
6.	Enicostema littorale	3 gm

Experimental procedure

1. MCF7 Human breast cancer cell line was procured from National center for cell sciences (NCCS), Pune maintained in DMEM medium supplemented with 10% fetal bovine serum.
2. Cells were incubated at a concentration of 1 × 104cells/ml in culture medium for 24 h at 37°C and 5% CO_2.
3. Cells were seeded at a concentration (70µl) 104cells/well in 100µl culture medium and 100µl Sample A (20 -100 µg/ml) into micro plates respectively (tissue culture grade, and 96 wells).
4. Control wells were incubated with DMSO (0.2% in PBS) and cell line. All samples were incubated in triplicate. Controls were maintained to determine the control cell survival and the percentage of live cells after culture.
5. Cell cultures were incubated for 24 h at 37°C and 5% CO_2 in CO_2 incubator (Thermo scientific BB150).
6. After incubation, the medium was completely removed and Added 20 µl of MTT reagent (5mg/min PBS)
7. After addition of MTT, cells incubated for 4 hrs at 37oC in CO_2 incubator.
8. Observed the wells for formazan crystal formation under microscope. The yellowish MTT was reduced to dark coloured formazan by viable cells only.
9. After removing the medium completely. Added 200µl of DMSO (kept for 10 min) and incubate at 370C (wrapped with aluminium foil).
10. Triplicate samples were analyzed by measuring the absorbance of each sample by a Elisa microplate reader (Benesphera E21) at a wavelength of 570 nm [16, 17].

Standardization of formulation: 1. Weight variation of capsule

weight 10 capsule (total weight) find out individual weight and calcaluate the average weight then individual weight of capsule should be with in the limit of average weight.Remove the net content of each capsule.weigh emply Shells individually. Find out net weight of content individually by using formule. Table no: 2.

Net weight (Avg. fill) = Avg. Wt - empty cap shell wt.
= 0.28 - 0.06.
= 0.22

2. Stability tests

Stability tests for capsules are performed to know the integrity of gelatin capsule shell (but not to know the stability of therapeuticallay active agent) and for determining the shelf life of capsules.The tests helps in improving the quality of contents of capsule shell and for choosing the appropriate retail package.

Before actually performing the tests following fact

The capsule shell are to be stabilized to know atmospheric condition with relative humidity about 20-30% and temperature about 21-24 °C.

A) Shell integrity test

This test is performed to find out the integrity of capsule shell. The standard capsule shells kept at the room temperature 40 °c and 80% RH becomes more soft, sticky and swollen.

B) Determination of shelf life

Shelf life or the expiry date of packed capsules is determined under normal storage conditions

3. Moisture permeation test

This test is carried out to assure the suitability of containers for packaging of capsules. The moisture permeating feature of capsules packaged in Single unit containers-blister pack or strip pack.Unit dose containers glass or plastic bottle is to be determined.

4. Identification of active compounds

Table 2: Effects of compound against MCF7 (Breast cancer cell line) by MTT assay

A] Sample description	Sample-A
B] Activity	Solid
C] Cell line	*In vitro* cell viability assay
D] Sample form	MCF 7 (HUMAN BREAST CANCER CELL LINE)
E] Media	▪ DMEM with high glucose (Cat No-11965-092), ▪ FBS (Gibco, Invitrogen) Cat No -10270106 ▪ Antibiotic – Antimycotic 100X solution (Thermo fisher Scientific)-Cat No-15240062

Result and Discussion

Table 3: Effects of compound against MCF7 (Breast cancer cell line) by MTT assay

Sr. No.	Concentration (14/m1)	Absorbance (0 D)				Cell inhibition (%)	ICSO (µg/ml)
		1	2	3	Average		
1.	5FU 10	0.394	0.465	0.393	0.417333	32.10412148	53.32
2.	20	0.48	0.376	0.34	0.398667	35.14099783	
3.	40	0.333	0.325	0.396	0.351333	42.84164859	
4.	80	0.292	0.241	0.208	0.247	59.81561822	
5.	100	0.189	0.186	0.124	0.166333	72.93926247	

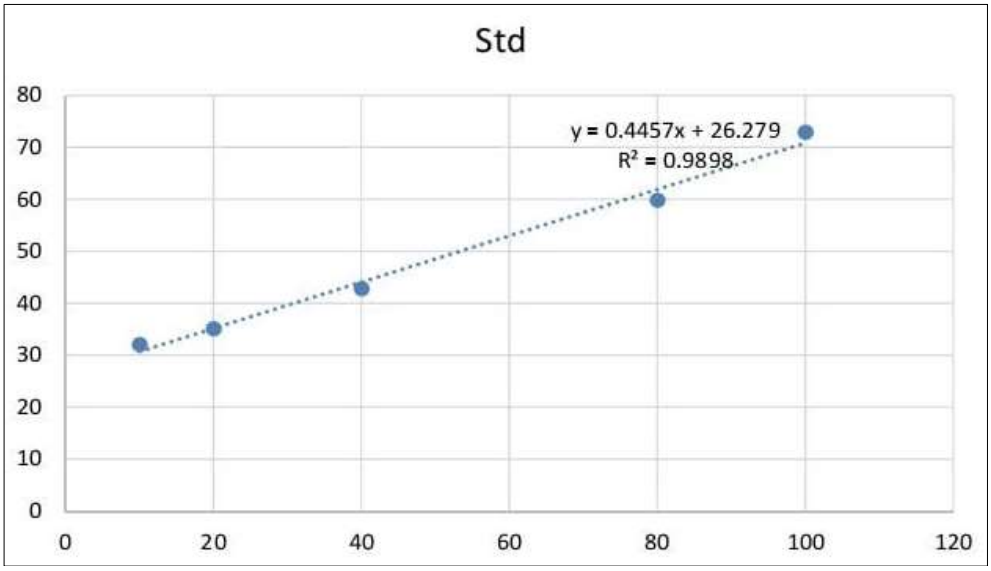

Fig 2: Effects of Sample A against MCF7 (Breast cancer cell line) by MTT assay (IC50=53.32)

Effects of Sample A against MCF7 (Breast cancer cell line) by MTT assay

Table 4: Weight variation of capsule

Sr. No.	Concentration (pg/ml)	Absorbance (0 D)				Cell viability (%)	Cell Inhibition (%)	IC50 (Rem!)
		1	2	3	Average			
1.	20	0.519	0.526	0.543	0.529	57.935	42.064	48.98
2.	40	0.459	0.454	0.468	0.460	50.383	49.616	
3.	80	0.359	0.435	0.411	0.401	43.962	56.037	
4.	100	0.337	0.362	0.316	0.338	37.030	62.969	

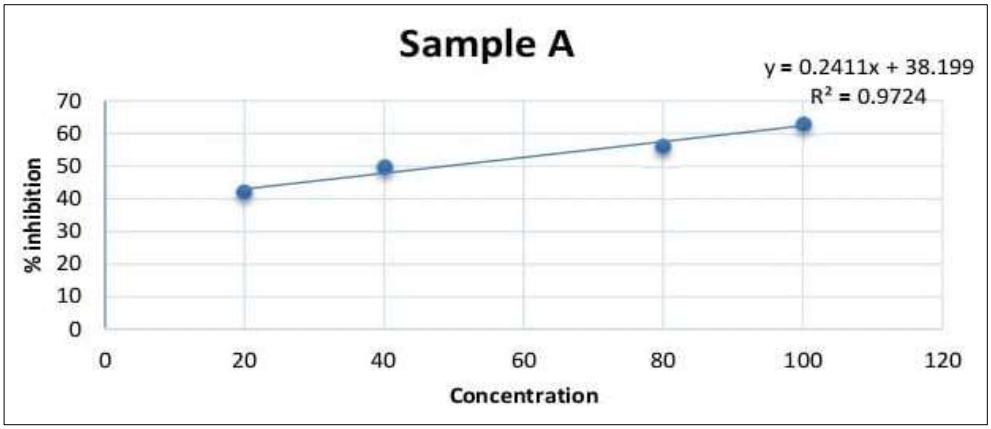

Fig 3: Effects of compound against MCF7 (Breast cancer cell line) by MTT assay (IC50= 48.98)

These results demonstrate that the created approach was easy to use, affordable, quick, and accurate. As the result shows that the value of y=0.4457x+26.279 and the slope is 0.9898 it's valid.

Table 5: Weight variation of capsule

Sr. No	Weight of Capsule
1.	0.33
2.	0.24
3.	0.27
4.	0.33
5.	0.31
6.	0.26
7.	0.31
8.	0.31
9.	0.34
10.	0.26

Table 6: Physicochemical properties of powder

Powder	
Flavor system	
Taste	better
Colour	Brown
Texture	Fine powder
Physical properties	
Size	No limit

Discussion

Cancer is treated by surgery, radiation therapy, chemotherapy, targeted therapy, Hormone therapy, Stem cell transplant, precision medicine and Immunotherapy to treat cancer. The study was conducted to annotate the immunomodulatory potential of Indian medicinal plants.

Conclusion

At the different doses (10 to 100 µg/ml) of Sample A carried out for anticancer activity against MCF-7 cell line, the compounds Sample a showed good activity against breast cancer cell line when you compared to standard drug 5 FU.

The use of various plant specific dose during the scheduled regimen may be helpful in obtaining higher protective antibody against different infections including production and development of more effective cell mediate immune response for protection against various types of cancer. Herbal formulation may be therefore recommended for use as positive immunomodulator.

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