

FORMULATION AND CHARACTERIZATION OF NUTRACEUTICAL HERBAL TABLET FOR TREATMENT OF CANCER PATIENT

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Abstract:

Nutraceuticals, mostly phytochemicals derived from dietary or medicinal plants such as soya bean, garlic, ginger, tea as well as propolis, honey and others, may have chemopreventive activities, as already suggested by epidemiologic and animal model studies. on immunity response of human body. Nutraceutical supplement are maintaining a healthy weight in cancer patients. Nutraceutical Herbs like Spirulina Powder, Turmeric Powder, Giloy Powder, Moringa Powder, Ginger powder, clove, funnel, liquorices, starch and other ingredients play a vital role in Cancer patient. Nutraceutical Formulation was formulated in the form of Tablets Formulation by making use of Spirulina Powder, Turmeric Powder, Giloy Powder, Moringa Powder, Ginger powder, Clove, Funnel, Liquorices, Starch, Microcrystalline cellulose, Croscarmellose sodium, Purified talc, magnesium stearate all the ingredients are collected from the local market having good quality. the present investigation revealed that on the basis of Pre-Compression and Post-Compression of Tablets and Initial Study F4 is superior and all the parameters are satisfactory results. The combination of chemotherapeutic agents with nutraceutical supplements in future novel horizons for more effective management of cancer patients.

Keywords: Herbal Tablet, Turmeric Powder, Giloy Powder, Moringa Powder, Ginger powder.

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Introduction

Cancer is a disease of uncontrolled growth of cells. It mainly caused by the misbalancing between apoptosis, check point and proliferation rate under the cell cycle. In normal body proliferation rate works normally and in cancer patient uncontrolled growth of cell or proliferation and dysfunctioning the apoptosis. The regulation of cell cycle depends on main three check points and those check points balancing the apoptosis and proliferation rate.¹ P₅₃ is a main check point for to regulate apoptosis and proliferation process. In apoptosis process P₅₃ containing the two types mechanism first is repair or fix problems and another is kill the cell. This three check point located between G₁ phase and S phase; second check point present between S and G₂ phase and third check point present in M phase. Cyclin and CDK it gives the important role to regulate the cell cycle. Cyclin and CDK work as to transfer the cell from one phase to another phase passing by check point. If cells are healthy then Cyclin through transfer the cell from one to another phase and cell are unhealthy then check point transfer cell for apoptosis process or repair the problem of cell. If this all cycle was disturbed then it causes the cancer. The three causing factors responsible for to produce cancer that are biological factors, physical factors and chemical factors. Eg EBV (Epstein - Barr virus) mainly target on ² genes and disregulate the apoptosis process. EBV target on MYC genes and BCL -2-L-11. MYC is a transcription protein (proteins). MYC contains the three type's chromosomes C-MYC, L-MYC, n-MYC. EBV act on C-MYC for causing cancer. BCL2-L-11 is regulating the Proapoptotic process and antiapoptotic process. BCL-2 play role as antiapoptotic in internal pathway of apoptosis process. Physical factors contribute to the development of cancer such as radiation, ionization. Ionizing radiation damages DNA. Ionizing radiation show direct effect and indirect effect on DNA. Due to direct effect damaged DNA and in indirect effect due to ionization formed free radicals and it's enhancing at high oxygen tension they cause DNA damage. After DNA damage they caused failed or aberrant repair cell and DNA repaired and tissue reconstitution. In aberrant repair they inhibit cell division caused cell death, fetus or germ cells: teratogenesis and due to additional transforming events formed carcinogenesis.³ The induction of cancer by chemical carcinogens occurs after a delay –weeks to months in the case of experimental animals, and often several years in humans. The mainly three stages in chemical carcinogenesis this are first initiation, second promotion and third progression stage shown in fig no 1.

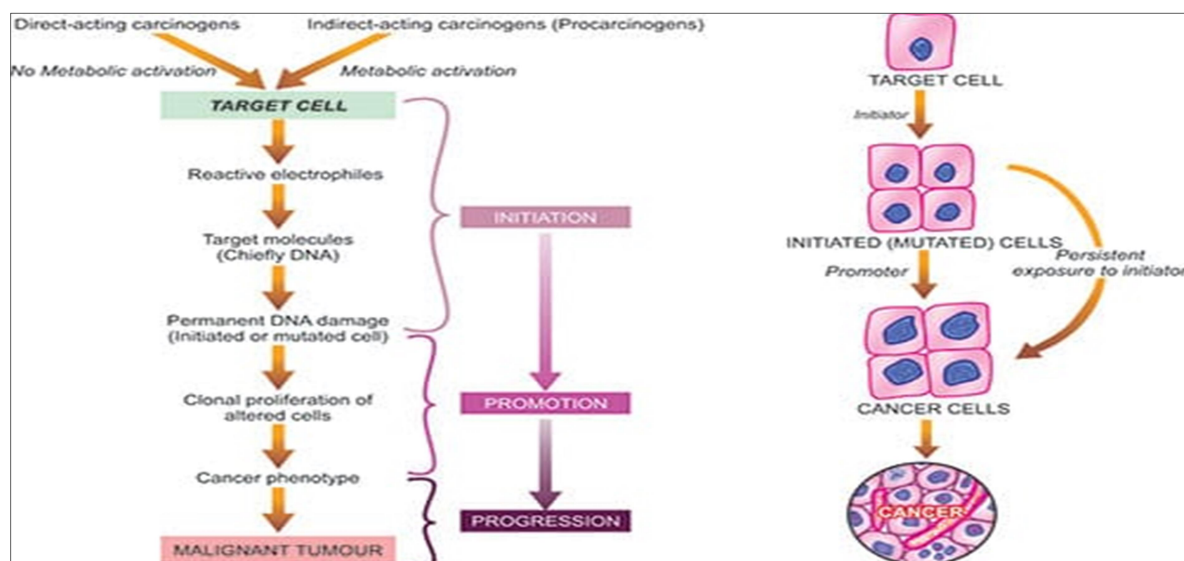


Fig no 1.Sequential stages in chemical carcinogenesis (left) in evolution of cancer (right).

Table No. 1. Nutraceutical ingredients with their therapeutic applications⁴

Sr. No.	Nutraceutical Ingredients	Therapeutic Applications
1.	Probiotics, Prebiotics	Bone and Joint Health
2.	Vitamins, Antioxidants	Cancer Risk Reduction
3.	Soya based ingredients	Cardiovascular Health
4.	Minerals	Maternal and Infant Health
5.	Nutritional lipids and oil	Immune system
6.	Fibers and carbohydrates	Energy and Eye Health
7.	Dairy base ingredients	Skin Health, Respiratory Health

MATERIAL AND METHOD

1 SPIRULINA

Spirulina is a blue green algae *Spirulina platensis* or *Spirulina maxima* which is a member of the family Oscillatoriaceae. ⁵Cyanobacteria also include unicellular organisms and all of them are not spiral shaped (*Spirulina* is spiral shaped). Among the microalgae, *Spirulina maxima*

(*Arthrospira axima*), *Spirulina platensis* (*Arthrospira platensis*), and *Spirulina fusiformis* (*Arthrospira fusiformis*) are the most widely cultivated species around the world and are widely used as health foods, food additives, and potential sources of high value chemicals and pharmaceutical metabolites⁶.

TAXONOMY

Table no.2.

Kingdom	Eubacteria
Subkingdom	Negibacteria
Class	Cyanophyceae
Order	Nostocales
Family	Oscillatoriaceae
Genus	Spirulina
Species	Arthrospira Spirulina



Figure No. 2. Spirulina Powder

2. TURMERIC

Turmeric is a spice derived from the rhizomes of *Curcuma longa*, which is a member of the ginger family (Zingiberaceae). Rhizomes are horizontal underground stems that send out shoots as well as roots.⁷ The bright yellow colour of turmeric comes mainly from fat-soluble, polyphenolic pigments known as curcuminoids. Curcumin, the principal curcuminoid found in turmeric, is generally considered its most active constituent.⁸ The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and zingiberone.⁹ Turmeric is a mild digestive, being aromatic, a stimulant and carminative. Turmeric is one of nature's most powerful healers. It contains not less than 1.5% of

curcumin. Turmeric contain about 5% of volatile oil, resin, zingiberaceous starch grain and yellow colouring substances known as curcuminoids (curcumin 50-60%). The active ingredient in turmeric is Curcumin. Turmeric has been used for over 2500 years in India, where it was most likely first used as a dye. Curcumin is one of the most researched bioflavonoids today and a number of studies have confirmed its antioxidant, anti-inflammatory, anti-cancer, chemo protective, gastro protective, and many other health properties. Studies have shown that it is not toxic, even at doses up to 12 g / day, and it is tolerated very well by the human body.¹⁰

Taxonomy

Table no 3.

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Asterales
Family	Asteraceae
Tribe	Heliantheae
Genus	Tridax
Species	T. Proc



Figure No. 3. Turmeric Plant

3. GINGER

Ginger is one of the most important and most widely used spices worldwide. Ginger botanically known as *Zingiber officinale* Rosc., belongs to family Zingiberaceae. The volatile oil components consists mainly of sesquiterpene hydrocarbons, predominantly zingiberene (35%), curcumene (18%) and farnesene (10%) Non-volatile pungent compounds include gingerols, shogaols, paradols and zingerone. Ginger contains fats, waxes, carbohydrates, vitamins and minerals. Ginger rhizomes also contain a potent proteolytic enzyme called zingibain. In ancient times ginger was more valued for its medicinal properties and played an important role in primary health care. Ginger was among the most highly valued of all mild carminatives and it was a component of many pharmaceutical preparations¹¹.

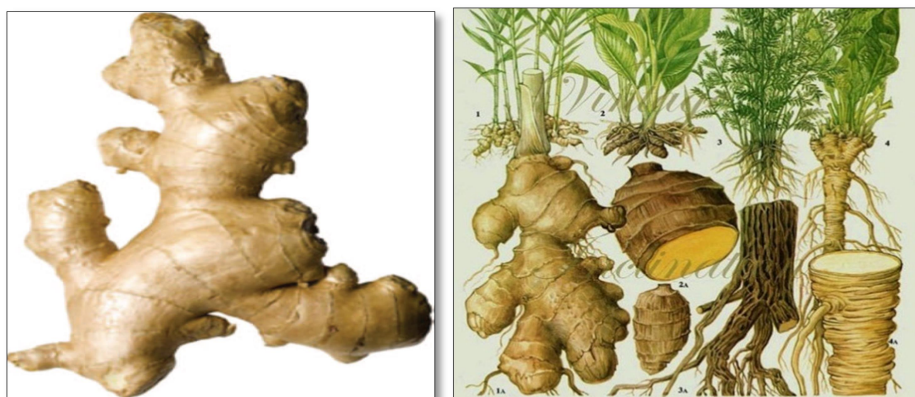


Fig No 3. Plant of ginger

4. GILOY

Tinospora Cardifolia is a climbing shrub belongs to family Menispermaceae. It is genetically diverse, large, deciduous climbing shrub with greenish yellow typical flowers, found at higher altitude. There are various species of *Tinospora*, of which *T. cardifolia* is the most extensively studied species for its biological activities¹². A variety of active components derived from the plant like alkaloids, steroids, diterpenoid lactones, aliphatics, and glycosides have been isolated from the different parts of the plant, like root, stem, leaves and whole plant. The qualitative analysis of giloy has shown the presence of alkaloids, flavonoids, glycosides, diterpenes, tannins, phytosterols, saponins, phenols resins, fixed oils, carbohydrates, proteins and amino acids. Different phytochemicals that have been isolated from giloe including alkaloid Choline,

Magnoflorine, Tinosporin, Palmatine, Isocolumbin, Aporphine, Jatrorrhizine, Tetrahydropalmatine, berberine, Tinocordiside, N-formylasimilobine 2-O- β -D-glucopyranosyl-(1 \rightarrow 2)- β -D-glucopyranoside (tinoscorside A, 1) and N-acetylasimilobine 2-O- β -D-glucopyranosyl-(1 \rightarrow 2)- β -D-glucopyranoside (tinoscorside B, 2), a new clerodanediterpene, tinoscorside C (3), and a new phenylpropanoid, sinapyl 4-O- β -D-apiofuranosyl-(1 \rightarrow 6)-O- β -D-glucopyranoside (tinoscorside D, 6), palmatine, tetrahydropalmatine, have been isolated from giloe. The glycosides Cordifolioside A, Tinocordiside, Syringin, 18-norclerodane glycoside were also isolated from giloe.¹³

Table No. 4. Taxonomy

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Menispermaceae
Genus	Tinospora
Species	Cardifolia



Fig No 4. Plant of Giloy

5. MORINGA

Moringa native part of Africa and Asia. All parts of the *Moringa* tree are edible and have long been consumed by humans. *Moringa oleifera* is the most widely cultivated species in the genus *Moringa*, the only genus in the plant family *Moringaceae*. *M. oleifera* can be grown in any tropical and subtropical regions of the world with a temperature around 25–35°C. It is rich source of Potassium, Calcium Phosphorus, Iron, Vitamin A and, Essential amino acids, Antioxidants etc.

Another 9-Octadecenoic acid (20.89%), L-(+) -Ascorbic acid- 2, 6-dihexadecanoate (19.66%), 14-methyl -8-Hexadecenal (8.11%), 4- hydroxyl-4-methyl-2-pentanone (7.01%), 3ethyl-2, 4-dimethyl-pentane (6.14%) and phytol (4.25%) as the major chemical constituents. It requires sandy or loamy soil with a slightly acidic to slightly alkaline pH and a net rainfall of 250–3000 mm. The direct seeding method is followed as it has high germination rates.¹⁴ Since Moringa seeds are expected to germinate within 5–12 days after seeding and can be implanted at a depth of 2 cm in the soil. Moringa can also be propagated using containers. The saplings are placed in plastic bags containing sandy or loamy soil. After it grows to about 30 cm, it can be transplanted. However, utmost care has to be taken while transplanting as the tap roots are tender and tend to get affected.¹⁵

Table No. 5. Taxonomy

Kingdom	Plantae
Divison	Angiosperm
Class	Eudicots
Order	Brassicales
Family	<i>Moringaceae</i>
Genus	<i>Moringa</i>
Species	<i>M. oleifera</i>



Fig No 5. - *Moringa oleifera lam*

6. FENNEL

Fennel is traditionally used for medicinal and culinary purposes. The entire plant is valuable in the medicinal industry; its enlarged base is used as a vegetable; its leaves are used for culinary purposes and its seeds as a spice and for essential oil extraction. The flowers and leaves are also used to make yellow and brown dyes. Fennel pollen is the most potent form of fennel, but it is extremely expensive. The genus *Foeniculum* (fennel) belongs to the family *Apiaceae*.¹⁶



Fig No5.6.1: Plant of fennel

7. CLOVE

The clove, *Syzygium aromaticum* (L.) Merrill et. Perry, belongs to the family *Myrtaceae*. The species is indigenous to certain volcanic islands of the North Moluccas (formerly known as the spice islands), in the eastern part of Indonesia where cultivated and wild forms are found. Volatile oil(15-20%), Eugenol (70-90), Acetyl Eugenol, α , β - Caryophyllene, Tannins and other substances mainly Methyl furfural and dimethyl furfural The tree is of medium size, is evergreen and reaches up to 20 m in height. Its canopy shape varies from cylindrical to pyramidal, depending on the variety. on-volatile resinous material, which accounts for the flavour mimicking the original ground spice.¹⁷

Table No. 6. Taxonomy

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Myrtaceae
Genus	Syrtaceae
Species	S. aromaticum

**Fig No.7. Plant of Clove****Pre-formulation study:****Preliminary Phytochemical Screening :**

As per the WHO Guidelines for quality standardization of Herbs and Herbal Formulation. The preliminary Phytochemical screening of herbs including Spirulina, Turmeric, Giloy, Ginger, Moringa, are carried out.¹⁸

Preparation and formulation of Nutraceutical powder-

Nutraceutical powder was prepared by mixing of Spirulina powder, turmeric powder, Giloy powder, ginger powder, Moringa powder with other ingredients. The prepared soup powders were then sealed in translucent or coloured polythene bag and used for chemical analysis.¹⁹

Table No. 7. Formulation of Nutraceutical Tablet

Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Spirulina	40	40	30	40
Turmeric	15	18	18	18
Giloy	40	40	50	40
Ginger	10	10	10	5
Moringa	25	25	25	30
Clove	9.5	9.5	9.5	9.5
Funnel	150	150	150	150
Liquorice	12.5	12.5	12.5	12.5
Starch	30	30	30	30
Microcrystalline cellulose	150	140	140	140
Croscarmellose sodium	15	20	20	20
Talc	1.5	2.5	2.5	2.5
Magnesium stearate	1.5	2.5	2.5	2.5
Total (mg/tab)	500	500	500	500

Evaluation of post-compression parameter:**A. Tablet thickness:**

Tablet thickness is an important characteristic in reproducing appearance. Three tablets were taken and their thickness was recorded by vernier caliper expressed in mm.²⁰

B. Tablet hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. Hardness of the tablets was determined by Monsanto hardness tester and the hardness should be found within the range of 5 to 5.5 kg/cm² for chewable tablet. Three tablets were randomly picked and analyzed for hardness.

C. Weight variation test:-

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the table. The weight variation test would be a satisfactory method of determining the drug content uniformity.

D. Friability test

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed.

The friability (F) is given by the formula,

$$\% \text{ friability} = \frac{\text{Initial weight} - \text{final weight}}{\text{Initial weight}} \times 100$$

A maximum loss of weight should not be greater than 1.0 percent is acceptable for tablets.

Stability study

These studies were carried out on Nutraceutical formulation by using REMI SC-6 plus stability chamber according to ICH guidelines. The accelerated stability conditions of 40 °C \pm 2°C with 70 \pm 5% RH for 90 days. The physical stability of nutraceutical formulation was observed periodically. The Nutraceutical formulation was evaluated after one month for the physiochemical parameter, flow property.

Preformulation study**Preliminary Phytochemical Screening:****Table No. 7. Phytochemical Screening**

Chemical compound	Test	Spirulina	Turmeric	Giloy	Moringa	Ginger
Test For Carbohydrates	Molisch's	+ve	+ve	+ve	+ve	+ve
	Fehlings	+ve	+ve	+ve	+ve	+ve
	Benedicts	+ve	+ve	+ve	-ve	+ve
	Iodine	+ve	+ve	-ve	+ve	+ve
	tannic acid	+ve	+ve	+ve	+ve	-ve
Test for Steroids	Salkowski reaction	-ve	-ve	+ve	-ve	+ve
	Libermann's reaction	-ve	-ve	+ve	-ve	+ve
Test for protein	Biurate	+ve	+ve	+ve	+ve	+ve
	Millon's	+ve	-ve	+ve	+ve	+ve

test for amino acid	Ninhydrin test for tyrosin	+ve	+ve	+ve	+ve	-ve
	Ninhydrin test for cysteine	+ve	+ve	+ve	+ve	-ve
Test for glycoside (cardic)	Legal's test for cardinolide s	+ve	-ve	+ve	+ve	-ve
	Test for deoxysugar	+ve	-ve	+ve	+ve	-ve
	Borntrager test	+ve	+ve	+ve	-ve	-ve
Test for glycoside	Borntrager test	+ve	+ve	+ve	+ve	-ve
Test for glycoside (saponin)	Foam test	+ve	+ve	+ve	-ve	+ve
Test for flavonoids	Shinoda test	+ve	+ve	+ve	+ve	+ve
	Sulphuric acid test	+ve	-ve	+ve	+ve	+ve
Test for	Dragendorff f's	-ve	+ve	+ve	+ve	+ve

Alkaloids	Mayer's	-ve	-ve	+ve	+ve	+ve
	Hager's	-ve	+ve	+ve	+ve	+ve
	Wagner's	-ve	+ve	+ve	-ve	+ve

Test for tannins and phenolic compound	5% FeCl_3 solution	-ve	-ve	+ve	+ve	-ve
	Lead acetate solution	-ve	+ve	+ve	+ve	-ve
	Bromine water	-ve	+ve	+ve	+ve	-ve
	Dilute HNO_3	-ve	+ve	+ve	+ve	-ve
Test for vitamin A	Test for Vitamin A	+ve	+ve	-ve	+ve	+ve
	Test for Vitamin C	+ve	+ve	+ve	+ve	+ve
	Test for Vitamin D	+ve	-ve	-ve	+ve	-ve

Where,

- absent , + present

Table No. 8. pH and viscosity of nutraceutical formulations

Formulation	Viscosity (cPs)	pH
	Mean±SD	Mean±SD
	Pre stability	Pre stability
	Mean±SD	Mean±SD
F1	602±4.84	4.1±0.20
F2	103±2.5	3±0.010
F3	600±4.80	4.1±0.19
F4	723±5.13	4.3±0.025
F5	629±4.92	4.2±0.020
F6	702±3.51	4.1±0.02

Nutraceutical powder formulation batches F1, F2, F3, F4 ,F5 and F6 combination were prepared and evaluated further by determining pH and viscosity. Formulations F1, F2, F3,F4,F5 shows change in pH, and viscosity Only F6 formulation shows pH range 4.1±0.02, and acceptable viscosity, with better stability.

Formulation, Development of Simple compress tablet

Evaluation of pre-compression parameter

Table No. 9. Pre-Compression Parameter

Formulation	Bulk density	Tapped density	Angle of repose(°)
	(gm/ml)	(gm/ml)	Mean±SD
	Mean±SD	Mean±SD	
F1	0.42±0.047	0.643±0.002	20.40±0.010
F2	0.39±0.017	0.682±0.002	20.42±0.015
F3	0.55±0.017	0.701±0.002	20.21±0.029
F4	0.54±0.017	0.712±0.002	20.53±0.02

Table No. 9. Carr's index and Hausner ratio

Formulation	Carr's index(%)	Hausner ratio (%)
F1	34.63	1.53
F2	42.81	1.74
F3	21.54	1.27
F4	24.15	1.3

Evaluation of post compression parameter**General appearance**

White to off white olive green colour, circular , one side split one plain tablet, surface texture proper

Post-Compression Parameter**Table No. 9. Hardness & Thickness of tablets**

Formulation	Hardness Mean (n = 3) ± SD (N)	Thickness Mean (n = 3) ± SD (mm)
	Pre stability Mean ± SD	Pre stability Mean ± SD
F1	62 ± 0.11	5.2 ± 0.2
F2	65 ± 0.16	5.3 ± 0.2
F3	59 ± 1.18	5.3 ± 0.4
F4	66 ± 0.17	5.2 ± 0.3

*All values are average of three determination (n=3)

Table No.10. Dimension & Friability of tablets

Formulation	Dimension Mean (n = 3) ± SD (mm)	Friability Mean (n = 3) ± SD (% w/w)
	Pre stability Mean ± SD	Pre stability Mean ± SD
F1	12.04 ± 0.12	0.36 ± 0.8
F2	12.01 ± 0.10	0.62 ± 1.2
F3	12.02 ± 0.08	0.59 ± 1.6
F4	12.00 ± 0.12	0.51 ± 1.0

*All values are average of three determination (n=3)

Table No. 11. Weight variation of tablets

Formulation	Weight variation Mean (n = 3) ± SD (mg)
	Pre stability Mean ± SD
F1	498.00 ± 1.68
F2	468.00 ± 1.35
F3	552.80 ± 1.25
F4	548.00 ± 0.84

*All values are average of three determination (n=3)

SUMMARY AND CONCLUSION:**Summary**

Nutraceutical supplementation seems to have a positive impact in cancer treatment. Particularly as an antioxidant, anticancer, immunomodulation even if the role of micronutrient in cancer remains controversial. The purpose of this study is to examine cancer in relation to chemotherapy effects on immunity response of human body. Nutraceutical supplement are maintaining a healthy weight in cancer patients. Nutraceutical Herbs like Spirulina Powder, Turmeric Powder, Giloy Powder, Moringa Powder, Ginger powder, clove, funnel, liquorices, starch and other ingredients play a vital role in Cancer patient. Nutraceutical Formulation was formulated in the form of Tablets Formulation by making use of Spirulina Powder, Turmeric Powder, Giloy Powder, Moringa Powder, Ginger powder, Clove, Funnel, Liquorices, Starch, Microcrystalline cellulose, Croscarmellose sodium, Purified talc, magnesium stearate all the ingredients are collected from the local market having good quality.

Conclusion:

The Safe and effective Nutraceutical formulation for Cancer patients of combined herbs, Nutraceutical herbs and spices, flavour, thickeners and other ingredients in the form of Tablets was successfully developed, the present investigation revealed that on the basis of Pre-Compression and Post-Compression of Tablets and Initial Study F4 is superior and all the parameters are satisfactory results. The combination of chemotherapeutic agents with nutraceutical supplements in future novel horizons for more effective management of cancer patients.

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