Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18538
DOI URL: http://dx.doi.org/10.21474/IJAR01/18538

REVIEW ARTICLE

POSITIVE IMPACTS OF PHYTOCHEMICALS AND THEIR BIOACTIVE COMPONENTS FROM PLANTS AGAINST HEPATOCELLULAR CARCINOMA - REVIEW

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Manuscript Info

Manuscript History
Received: 15 February 2024
Final Accepted: 19 March 2024
Published: April 2024

Key words:-
Herbal Plants, Liver Cancer, Bioactive Components

Abstract

The terrible nature of the condition and the lack of an effective, long-lasting treatment, anticancer therapy has become one of the biggest issues in the medical field. In light of this, it is believed that discovering an effective drug is a popular research issue in the field of medical science. There is a long history of using plant-derived extracts, mixtures, fractions, and phyto-chemicals to treat liver issues. The goal of this study is to assess the scientific research on the efficacy of various bioactive compounds that have been isolated from plant extracts over the past 20 years against the fatal disease, hepatocellular carcinoma (HCC). The knowledge at hand includes a number of research and tests employing plant parts such as stems, leaves, roots, flowers, fruits, bark etc. And we could deduce from the literature that the researchers conducted in-vitro, in-vivo, ex-vivo, and other types of experiment using these extracts to obtain the best outcomes. This study aims to assess the level of progress made in the quest for a suitable, long-lasting natural treatment for HCC and makes an effort to compile a list of plants that have been shown to have hepato-protective properties. Finding new anticancer drugs derived from natural resources will receive more focus.

Introduction:-

Hepatocellular carcinoma (HCC), is a very common form of liver disease, is one of the main factors contributing to cancer-related mortality around the world. HCC also referred to as malignant hepatoma, is a primary liver cancer that develops as a result of hepatic inflammation. It is also more likely to develop in people with chronic liver conditions like non-alcoholic fatty liver disease, severe drinking habit and diabetes, cirrhosis brought on by hepatitis B or C, and cirrhosis itself (Manimekalai et al., 2016; Rajesh et al., 2016; Hemalatha et al., 2020; Flora Priyadharshini et al., 2020; Rajesh and Sivakumari, 2020; Perumal et al., 2021; Padmavathy et al., 2021; Sivakumari et al., 2022). Even if the illness's diagnosis and treatment have improved, the prognosis is still not good. Although satisfactory outcomes are obtained with treatments like chemotherapy and anticancer medications, these methods also have some toxicity and side effects (Hassan et al., 2017). Surgical excision, liver transplantation, interventional therapy, loco regional ablation, trans-arterial chemo-embolization, chemotherapy with sorafenib, radiation, immunotherapy, etc. are a few treatment options for the disorder. These treatments and drugs may facilitate curing cancer, but they also carry a risk of serious side effects, including alopecia, diarrhea, allergies, hyper-bilirubinemia,

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tiredness, and skin rashes or diseases of the hands or feet (Cheng et al., 2020). The demand for the discovery of anticancer drugs with more efficacy, fewer side effects, and lower cost appears to be growing in light of the risks and side effects associated with the present cancer therapies.

Plants are the sole best choice since they are an inexhaustible supply of powerful chemotherapeutic chemicals to cure the illness (Jung et al., 2015). Products made from plants, such as bioactive chemicals, serve as a reservoir for the action and evolution of anticancer chemotherapy medicines. The identification and isolation of the bioactive chemicals that are efficient for the therapy of HCC has been the subject of extensive research and study over the past few decades. Since ancient times, plants have been employed for therapeutic purposes. There is proof that herbal medicine has been used by Indian Vaids, Unani Hakims as well as European and Mediterranean cultures. There were some medical systems like Ayurveda, Unani and Chinese Medicine, etc., created by some indigenous civilizations. Societies like Rome, Egypt, Iran, Africa, and America have often employed herbal medicines. India has a rich source of medicinal plants and Indian forest is the major source of plenty of medicinal herbs. Ayush systems in India contain information about 8,000 herbal remedies. The key indigenous medical systems of Ayurveda, Unani, Siddha, and Folk (tribal) Medicines are seem to be identical (Manimekalai et al., 2016).

People all across the world are experiencing terrible conditions as a result of the deadly disease known as cancer. Technology advancements could detect the disease and treat it more successfully than before. However, without a complete cure, it still has the potential to kill the majority of those who are affected. Due to the lack of faith in the effectiveness of treatment, most of the cancer patients, even after surviving the initial cancer attack, admit their death since there is a chance that the disease might return. As a result, the patient continues to live under the shadow of the disease even after recovering from the disease. Widening the gap between man's understanding of himself and the environment, the current chaotic way of life, the pollution brought on by rapid industrialization and infrastructure developments, all these have significantly increased the number of cancer patients worldwide. Therefore, the purpose of this review is to assess the progress made in finding a treatment for HCC that is sustainable and uses plant-based bioactive chemicals. By reviewing the literature that has been published between 2000 and 2022, it is possible to compile a list of the bioactive chemicals that have been discovered and isolated from plant extracts.

Methodology:-

To conduct the review, secondary data was gathered from the body of previously published literature, including books, journals, articles, and research papers. The literature contains secondary data on the specifics of plant part extracts (stalk, root, flower, fruit, fruit peel, stem bark, seeds, latex, etc.) from native, tropical, herbal plants. Those extracts were tested in various ways (in vivo, in vitro, ex vivo, etc.) to identify the phytochemicals that are effective against the disease. Based on the extract obtained from the section of the plants utilized for the study, this aggregated data is examined and organized into categories. Such categorization makes data reading and assessment most efficient and simple.

Results:-

Cancer has become the leading cause of mortality and illness, and it has a major global health concern. Research conducted in 2012 and a report named "World cancer report" published in 2014 suggested that there were 14.1 million new cases of cancer, 18.2 million cancer-related deaths, and 32.6 million people living with cancer globally. Men were affected more with cancer than women (7.4 million for men and 6.7 million for women). The report has given an alarming prediction that there will be 24 million incidences by the end of 2035, which is terrifying (Casuga et al., 2016). Therefore, it is important to find a secure and long-lasting replacement for the treatment. The aforementioned research and scientific investigations have demonstrated that some plants which have medicinal properties can be used effectively to treat and prevent this disease with little to no side effects. The affordability, lack of adverse effects, and availability of naturally derived medicines have led to an increase in their use.

The examination of the acquired secondary data has produced extracts that may help in the separation of medications for the treatment of HCC. Following are categorizations and tabulations of the extracted materials:

1. Phytochemicals and their bioactive components from leaves of plants (Table 1)
2. Phytochemicals and their bioactive components from fruits of plants (Table 2)
3. Phytochemicals and their bioactive components from fruit peel of plants (Table 3)
4. Phytochemicals and their bioactive components from seeds of plants (Table 4)

5. Phytochemicals and their bioactive components from flowers of plants (Table 5)
6. Phytochemicals and their bioactive components from flower stigma of plants (Table 6)
7. Phytochemicals and their bioactive components from aerial parts of plants (Table 7)
8. Phytochemicals and their bioactive components from latex of plants (Table 8)
9. Phytochemicals and their bioactive components from roots of plants (Table 9)
10. Phytochemicals and their bioactive components from stem and bark of plants (Table 10)
11. Phytochemicals and their bioactive components from whole parts of plants (Table 11)

Table 1:- Phytochemicals and their bioactive components from the leaves of plants.

Sl. No	Plant	Active Compounds	Cell line or animal used for testing	Result	Author and year
1	Senecio latifolius	Pyrrolizidine, Retrorsine.	HuH-7 cells (in vitro)	1. The extract either caused micronuclei death or aberrant multinucleate cells. 2. Caused cells that were dividing to produce abnormal spindles. 3. Significant impacts on cytoplasmic tubulin with intra-cellular architectural rearrangements.	Steenkamp et al., 2001
2	Ceratonia siliqua	Catechins, Proanthocyanidin, Heaflavins, Gallic acid, Chlorogenic acid, Caffeic acid.	HCC in rat (in vivo)	1. Inhibited cell proliferation of HCC cells. 2. Cell lines underwent apoptosis.	Corsi et al., 2002
3	Caesalpinia bonducella	Flavonoids, Triterpenoids.	NDEA induced HCC in rat	1. Displayed an increase in antioxidants and decrease in lipid peroxidation. 2. Showed hepato-protective effects by reducing serum enzyme activities, elevation of proteins etc.	Gupta et al., 2005
4	Moringa oleifera	Phenolic compounds (Glycosides), Flavonoids.	HepG2 cells (in vitro)	1. Antioxidant activity, inhibition of radical formation. 2. Destruction of lymphoblasts. 3. Viability of HpG2 tumor cells were significantly affected.	Khalafalla et al., 2010
5	Corchorus olitorius	Phytol, Monogalactosyl, Diacylglycerol.	HepG2 cells (in vitro)	1. DNA fragmentation in HepG2 cells caused cell death. 2. Produced cytotoxicity that was mediated by a mitochondria-dependent apoptotic mechanism in HepG2 cells.	Li et al., 2012
6	Abrus precatorius	Polyphenol, Flavonoids.	HepG2 cells (in vitro)	1. Showed strong antioxidant activity, efficiently scavenging a variety of free radicals.	Gul et al., 2013

				2. Inhibition of tumor cell proliferation.	
7	Cynara scolymus	Inulin, Polyphenols, Hydoxycinnamate, Flavones.	HepG2 cells (in vitro)	1. The extract revealed anti-oxidant properties. 2. Highest anti-tumor activity but with toxicity for normal cells.	Pereira et al., 2013
8	Morus alba	Phenolic acids, Flavonoids, Anthocyanins.	HepG2, Hep3B cells in male Wistar rats (in vivo)	1. Modulate biochemical indicators and decreased NF-jB gene expression in order to stop the proliferation of HepG2 cells. 2. The extract caused apoptosis. 3. Displayed effects on acute liver failure that were hepatoprotective.	Fathy et al., 2013
9	Costus speciosus	Polyphenols, Carotenoids, Alkaloids, Diosgenin.	HepG2 cells (in vitro)	1. Displayed a remarkable reduction in cell viability. 2. Bioactive compounds had disturbed, modulated the cell cycle and regulated signal molecules in the induction of apoptosis in HepG2 cells.	Nair et al., 2014
10	Piper krukoffii	Phenolic acid, Gallic acid, Flavanol, Catechin, Epicatechin.	HepG2 cells (in vitro), McA-RH7777 cells (in vivo)	1. The extract showed intracellular accumulation of reactive oxygen species (ROS). 2. Stimulated cytotoxicity to rat hepato carcinoma cells - McA-RH7777.	Lizcano et al., 2014
11	Piper putumayo	Phenolic acid, Gallic acid, Flavanol, Catechin, Epicatechin.	HepG2 cells (in vitro), McA-RH7777 cells (in vivo)	1. Showed cytotoxicity to rat hepatoma in McA-RH7777 cells with an intracellular accumulation of reactive oxygen species (ROS).	Lizcano et al., 2014
12	Vismia baccifera	Flavanol, Catechin, Epicatechin, Phenolic acid, Gallic acid.	HepG2 cells (in vitro), McA-RH7777 cells (in vivo)	1. Showed the selective killing of HepG2 cells. 2. Promoted cytotoxicity to rat hepatoma McA-RH7777 cells with an intra-cellular accumulation of reactive oxygen species.	Lizcano et al., 2014
13	Aloe vera	Anthraquinone (Aloeemodin, Aloin, Barbaloin, Anthranol, Emodin).	HepG2 cells (in vitro)	1. Displayed increased cytotoxicity against HepG2 cells 2. It does modulation of apoptosis and induced apoptosis and autophagy.	Shalabi et al., 2015

14	Broussonetia luzonica	Propanetriol, Monoacetate, Phytol, Squalene.	HepG2 cells (in vitro)	1. Exhibited marked inhibition of HepG2 cell proliferation.	Casuga et al., 2016
15	Cardiospermum halicacabum	Stearic acid.	HepG2 cells (in vitro)	1. Stearic acid acted as a potential and natural therapeutic agent against HCC. 2. The leaf extract showed inter-action with transferrin proteins responsible for hepatocarcinoma.	Rajesh et al., 2016a; Rajesh et al., 2016b
16	Origanum majorana	Flavonoid, (Luteolin, Apigenin, Tannins, Hydroquinone), Terpenoids (Thymol, Carvacrol) Phenolic glycosides (Arbutin, Orientin, Vitexin).	HepG2 cells (in vitro)	1. Exhibited a highly significant inhibitory effect on HepG2 cell proliferation which was evidenced by a reduction in viable cell count. 2. Extracts suppressed the activity of NF-kB gene expression of HepG2 cells.	Fathy et al., 2016
17	Brassica oleracea	Polyphenolics, Glucosinolates, Carotenoids, Flavonoids (Lutein, Quercetin, Kaempferol and Rutin), Gallic acids, Caffeic acids.	HCC in rat (in vivo)	1. Revealed mild kupffer cells activation. 2. Extract helped to regain the healthy hepatic histological structure.	Rezq et al., 2017
18	Cassia fistula	Phenols, Tannins, Flavonoids, Coumarins, Cardiac glycosides, Saponins, Quinones, Triterpenoids.	HepG2 cells (in vitro)	1. Exhibited good hepato-protective effect. 2. Inhibited cell proliferation through the induction of apoptosis in HCC cells.	Al Ssadh et al., 2018
19	Passiflora edulis	Polyphenols.	HepG2 cells (in vitro)	1. Significantly increased the cytotoxicity by the leaf extract. 2. Extracts significantly increased pro-apoptotic activity.	Aguillón et al., 2018
20	Zanthoxylum zanthoxyloides	Terpenoids, Alkaloids, Saponins, Tannin, Flavonoids, Phenol.	CCl 4 /olive oil-induced HCC in rats (in vivo)	1. Reduced the mean tumor multiplicity significantly. 2. Significant improvement in liver histology and thus increased in the survival rate of the rats.	Barffour, 2019
21	Moringa	Phenolics,	HepG2 cells	1. The percentage of apoptotic	Mansour

	peregrina	Thymol, Ascorbic acid, Myristic acid, Palmitic acid, Linoleic acid, Retinol.	(in vitro)	HepG2 cells increased. 2. Apoptosis by up-regulation of p53, BAX, CASP3 and down-regulation of BCL-2 and MMP1. 3. Extract induced cell cycle arrest at S or G2/M phase.	et al., 2019
22	Vitis vinifera	Gallic acid, Polyphenols, Flavonoids.	HepG2 (in vitro)	1. Extracts showed high capability to scavenge DPPH. 2. Extracts have the ability to quench OH radicals, are common reactive oxygen species cause oxidative cell damage. 3. Extract have an anti-proliferative effect on HepG2 cells.	Ferhi et al., 2019

Table 2:- Bio active components derived from fruits of plants.

Sl. No	Plant	Active Compounds	Cell line or animal used for testing	Result	References
1	Lycium barbarum	Polysaccharides, Flavonoids, Carotenoids.	Rat (H-4-II-E) cells (in vivo), HA22T, VGH, HepG2 cells (in vitro)	1. Dose-dependently inhibited proliferation of H-4-II-E cells. 2. Inhibited proliferation and stimulated p53-mediated apoptosis in HCC cells.	Chao et al., 2006
2	Ziziphus mauritiana	Triterpenoids, Alkaloids, Phenolics, Catechins, Flavonoids, Saponins, Tannins.	P-DAB induced HCC in rat (in vivo)	1. Significant recovery from p-DAB + PB intoxicated liver damage.	Kalidoss and Krishnamoorthy 2011
3	Allium sativum	Alliin, Allicin, Ajoenes, Vinyldithiins, Flanoids, Quercetin.	NDEA induced HCC in rats (in vivo)	1. The extract enhanced the antioxidant activity. 2. It possess a property to induce apoptosis in the hepatoma cells.	Zhang et al., 2012
4	Citrullus colocynthis	Triterpene, Glucoside, Cucurbitacins, Cucurbitacin E glucoside, Cucurbitacin I glucoside.	HepG2 cells (in vitro)	1. Exhibited potent cytotoxicity in vitro against HepG2 cells. 2. The hematological parameters were restored and liver enzyme ALT reached to normal levels.	Ayyad et al., 2012
5	Averrhoa carambola	Catechin, Epicatechin,	DENA induced and CCl 4 -	1. Improved level of GSH, CAT, SOD and total	Singh et al., 2014

		Proanthocyanidins, Saponins, Ascorbic acid.	promoted liver cancer in Swiss albino mice (in vivo)	proteins induced by DENA in liver tissue. 2. Reduced hepatic lipid peroxidation which cause mutagenesis and carcinogenesis.	
6	Capsicum chinense	Phenol, Capsaicinoids, Capsaicin Anddi-hydrocapsaicin.	HepG2 (in vitro)	1. Showed the anticancer properties by modulating the free radicals release. 2. It induced apoptosis through increased intracellular ROS and calcium levels.	Amruthraj et al., 2014
7	Ligustrum lucidum	Cisplatin, Doxorubicin, SN-38, Camptothecin.	Bel-7402 cells (in vitro)	1. Induced apoptosis and cell senescence through upregulation of p21. 2. Caused morphologic cellular changes, and cell cycle arrest occured at G0/G1 phase in Bel-7402 cells.	Hu et al., 2014
8	Punica granatum	Ellagitannins, Flavonoids.	N-nitrosodiethylamine (NDEA) induced-HCC in rat (in vivo)	1. Antioxidant activity, radical scavenging capacity, chemo-preventive and anti-apoptotic properties were observed. 2. Suppressed chemically induced cancer. 3. Reduced the activities of the elevated enzymes like AST, ALT and ALP.	Hussein et al., 2014
9	Rubus occidentalis	Anthocyanins.	HepG2 cells (in vitro)	1. Reduced bad cholesterol, increased good cholesterol by lowering the gene expression. 2. Down-regulation of SREBP-1c caused damage control in fatty liver disease.	Moon et al., 2014
10	Garcinia dulcis	Furandione, Xanthones, Flavonoids, Dulcisflavan, Mangostin, Dulcisxanthone.	HepG2 cells (in vitro)	1. Stimulated cyto-toxicity and Apoptosis in HepG2 cells. 2. Showed antioxidant and anticancer properties.	Abu Bakar et al., 2015
11	Olea europaea	Oleanolic acid.	HepG2 cells (in vitro)	1. Inhibition in the growth of HepG2 cells. 2. Induced cytotoxic effect against HepG2 cells.	Zhu et al., 2015

				3. Apoptosis was induced.	
12	Elettaria cardamomum	Gallic, Tannin, Caffeic, 4,5-dicaffeoyl quinic acid.	DENA induced HCC in rats (in vivo)	1. Reduced liver injury and inhibited effect of DENA. 2. Increased activities of anti-oxidant enzymes and possess chemo preventive anticancer effect.	Elguindy et al., 2016
13	Garcinia mangostana	Phenolic acids, Xanthones, Anthocyanins, Procyanidins, Anthocyanin - Cyanidin-3-sophoroside.	HepG2 cells (in vitro)	1. Affected cell cycle and induced apoptotic pathways. 2. Inhibition of cell viability of HepG2 cells.	Manimekalai et al., 2016
14	Elaeagnus angustifolia	Phenolic acids, Flavonoids, Hydroxycinnamic acid, Benzoic acid, Caffeic acid.	Di-ethyl-nitrosamine (DEN) induced HCC in rats (in vivo)	1. Prevented lipid per-oxidation in the liver tissues. 2. Prevented the increase in relative liver weight as a prognostic marker of HCC.	Amereh et al., 2017
15	Litchi chinensis	Polyphenols, Gallic acid, Chlorogenic acid, Catechin, Caffeic acid, Epicatechin, Rutin.	Human HCC (HepG2) cells (in vitro)	1. Protected from stress-induced damage by increasing activity of free radicals scavenger enzymes and reduced mitochondrial reactive oxygen species (ROS). 2. Rutin exhibited antitumor properties by inhibiting prolife-ration, attenuating super-oxide anion production and affecting migration of cells.	Emanuele et al., 2017
16	Phoenix dactylifera L	Sterols, Polyphenols Flavonoids (Apigenin, Quercetin, Luteolin), Glycosides.	DEN-induced hepatic cancer in Wistar albino rats (in vivo)	1. Cell cycle inhibition, induction of apoptosis. 2. Restored normal liver structure, oxidative marker level and cytokines balance. 3. Reversal of the toxic effects of DEN.	Khan et al., 2017
17	Physalis peruviana	Organic acids, Phenolic compounds, Carotinoids, Glycosides, Coumarins, Flavonoids.	HCC in male albino rats (in vivo)	1. Modulation and arrest in hepatic cell cycle. 2. Homeostatic state evidenced for liver cell apoptosis and stabilization of DNA. 3. Inhibited cell proliferation in a dose and	Hassan et al., 2017

				time-dependent manner and stimulate apoptosis by the release of cytochrome c.	
18	Lonicera caerulea	Anthocyanin - Cyanidin-3-O-glucoside (C3G) Proto-Catechuic Acid (PCA), Phloro-Glucin-Aldehyde (PGA).	HepG2 cells (in vitro)	1. Reduced cell viability of HepG2 cells. 2. Produced a time- and dose-dependent inhibition of HepG2 cell proliferation.	Pace et al., 2018
19	Passiflora edulis	Polysaccharides.	HepG2 cells (in vitro)	1. Significant decrease in cell viability was observed. 2. Significant increase in cytotoxicity by extract. 3. Both extracts increased pro-apoptotic activity.	Aguillón et al., 2018
20	Alpinia oxyphylla	Yakuchinon A and B, Oxyphyllacinol, Nootkatone, Tectochrysin, Chrysin, Terpenoids.	BEL7402, HepG2, SMMC-7721, Hep3B, l HL-7702 cells (in vitro), Hep3B injected nude mice (in vivo)	1. Viability of cancer cells decreased. 2. Inhibited the growth of HCC-Hep3B cells. 3. Apoptosis or cell death was induced in Hep3B cell in vitro.	Hui et al., 2019
21	Cydonia oblonga	Phenolic acids, Flavonoids, Quercetin, Galactoside, Rutin, Caffeoylquinic acids, Kaempferol, Rutinoside, Glucoside.	DEN induced HCC in rats (in vivo)	1. Reducedthe levels of serum biomarkers of liver damage and cancer. 2. It exhibited chemopreventive effect and hepato-protective effect against HCC in rats.	Adiban et al., 2019
22	Gleditsia sinensis	Triterpenes, Sterol, Flavonoids, Alkaloids, Phenolics (Cytochalasin).	Male weaned Wistar rats with Walker-256 cancer cell line (in vivo)	1. Promoted apoptosis by inhibiting telomerase activity. 2. Showed activation of tumor suppressor genes and inactivation of oncogenes.	Cai et al., 2019
23	Paulownia tomentosa,	Pentacyclic triterpene, Ursolic acid.	HepG2 cells (in vitro), NDEA induced HCC in rats (in vivo)	1. Induced apoptosis in HepG2 cells in dose-dependent manner, DNA fragmentation, enhanced release of cytochrome c, activation of Caspase-3 etc. 2. Inhibited tumor invasion by inhibition of MMP-2, MMP-9.	Ali et al., 2019
24	Persea americana	Oleic acid, Palmitic acid.	HepG2 cells (in vitro)	1. Affected cell cycle arrest, retarded development and activated apoptosis.	Alkhalaf et al., 2019

				2. Showed significant inhibition of HCC in HepG2 cells.	
25	Xanthium strumarium	Glycosides, Phytosterols, Phenolic acids, Xanthiazone.	Huh-7, Hep3B cells (in vitro)	1. Inhibited cell proliferation through the apoptosis in HCC cells.	Kim et al., 2019
26	Annona muricata	Flavonoids, Phenols, Saponins, Tannins, Terpenoids, Triterpenoids.	HepG2 cells (in vitro)	1. Exhibited anti-proliferative activity in HepG2 cells on treating with extract. 2. Induced apoptosis in HepG2 cells by an intrinsic pathway related to cytochrome c migration to the cytosol and the dissociation of the mitochondrial membrane.	Hemalatha et al., 2020
27	Morus alba	Polyphenols, Flavonoids, Flavanols, Anthocyanins.	DEN-induced HCC in male Wistar rat (in vivo) HepG2, Hep3B cells (in vitro)	1. Reduced serum ALT and AST, Autophagy HCC marker, cleavage caspases, Ser-15-p53 and Ser46-p53 induced by DEN. 2. Inhibited the cell growth of HepG2 cells and Hep3B cells.	Cheng et al., 2020
28	Nephelium lappaceum	Alkaloids, Anthocyanins, Cardiac glycosides, Coumarin, Flavonoids, Phenols, Quinone, Saponin, Tannins, Terpenoids.	HepG2 cells (in vitro)	1. Showed an anti-proliferative effect on HCC cells. 2. The shrinkage of the HepG2 cells from polygonal to spherical shape was observed. 3. It also caused Nuclear as well as DNA damage.	Angalammal et al., 2021
29	Hylocereus undatus	Tannins, Phenols, Saponins, Squalene, Anthocyanin, Quinones, Cardiac glycosides, Terpenoids, Coumarins, Flavonoids, Rhodoxanthin.	HepG2 cells (in vitro)	1. Anti-proliferative effects of the extract was observed in HepG2 cells. 2. Dose and time-dependent orphological changes occurred in HepG2 cells. 3. Showed nuclear condensation and apoptosis.	Padmavathy et al., 2021, 2022

Table 3:- Phytochemicals and their bioactive components from fruit peel of plants.

Sl. No	**Plant**	**Active compounds**	**Cell line or animal used for testing**	**Result**	**Author and Year**

1	Ceratonia siliqua	Gallotannins, Gallic acid, Flavonoids, Proanthocyanidin, Chlorogenic acid, Caffeic acid.	Mouse HCC cell line (in vitro)	1. Inhibited cell proliferation of HCC cells. 2. Induced apoptosis in T1 cell lines.	Corsi et al., 2002
2	Litchi chinensis	Epicatechin, Proanthocyanidin B2 and B4.	HepG2 cells (in vitro)	1. Exhibited anticancer activity against HCC in vitro and in vivo by inhibition of proliferation and induction of apoptosis of cancer cells.	Wang et al., 2006
3	Ribes nigrum L	Flavonoids, Anthocyanins Phenolic acids, Proanthocyanidins.	HepG2 cells (in vitro)	1. Inhibited the proliferation of HepG2 cells. 2. Reduced the viability of human HepG2 cells.	Bishayee et al., 2010
4	Akebia quinata	Saponins, Oleanolic acid, Hederagenin, Saponin C.	HepG2 cells (in vitro)	1. Showed the inhibitory activity on HepG2 cells. 2. Induced apoptosis of HepG2 cells via., activation of Capase-3.	Kang et al., 2010
5	Carica papaya	Flavonoids, Glycosides, Tannins, Saponins, Alkaloids.	HepG2 cells (in vitro)	1. Extract conferred noticeable cytotoxicity against the HeG2 cancer cell line.	Garg et al., 2016
6	Garcinia mangostana	Xanthone, Garcinone E, Gartanin, Tovophyllin A, Alpha & Gamma Mangostin. Phenolic acid, Protocatechuic acid.	Hepatoma cell lines – HEp3B, HCC36,TONG, HA22T, HepG2 and SK-Hep-1 cells (in vitro)	1. Affected cell cycle and induced apoptotic pathways in the cell lines. 2. Inhibition of cell viability of HepG2 cells.	Manimekalai et al., 2016
7	Vitis vinifera	Phenolic compounds, Anthocyanin (Cyanidin, Petunidin, Peonidin, Malvidin), Quercetin, Hispidulin.	HepG2 cells (in vitro)	1. Decreased the viability of HepG2 cell line. 2. Induced significant cytotoxic effects and cell death mainly by necrosis.	De Sales et al., 2018
8	Punica granatum	Tannins, Flavonoids, Polyphenols, Anthocyanins, Cyanidins.	DEN induced HCC in rats (in vivo)	1. Extract exhibited good hepato productivity against DEN induced hepatocellular damage in rats.	Kumar et al., 2019
9	Solanum melongena	Glycoalkaloids (Solasonine, Solasodine, Solamargine).	Huh7, HepG2 cells (in vitro)	1. Induced anti-proliferative effect against liver cancer which attributed to cell cycle arrest at S-phase. 2. Induced significant	Fekry et al., 2019

				apoptosis in the cell lines.	

Table 4:- Phytochemicals and their bioactive components from seeds of plants.

Sl. No	Plant	Active compounds	Cell line or animal used for testing	Result	Author and Year
1	Coix Lacryma	Phenolic acids (Coumarin, Syringic, Ferulic, Vanillic acids), Flavonoids (Quercetin, Luteolin, Apigenin), Fatty acids (Oleic, Linoleic acids).	HepG2 cells (in vitro)	1. Cell arrest occurred in G2+M phase, thus less number of cells entered to G0 and G1 phase, and thus prevented hyperplasia and caused apoptosis. 2. The expression of caspase-8 caused apoptosis in HepG2 cells.	Lu et al., 2011
2	Akebia trifoliate	Bortezomib, Cannabinoids, Triterpenoid Saponin.	HepG2, HuH7, SMMC-7721 cells (in vitro)	1. Endoplasmic reticulum stress was induced. 2. Induced the emergence of apoptotic body. 3. Viability of cell decreased.	Lu et al., 2014
3	Citrus limon	Hesperidin, Neohesperidin, Naringin.	HepG2 cells (in vitro)	1. Induced both mitochondrial and death receptor pathways to promote cell apoptosis. 2. It possesses a high potential as an anticancer agent.	Banjerdpongchai et al., 2016
4	Litchi chinensis	Saponins, Flavonoid, Glycosides, Litchioside, Taxifolin-g lucopyranoside, Kaempferol neohesperidoside.	HepG2 cells (in vitro)	1. Reduced proliferation of cells and appearance of apoptotic morphological features. 2. Affected the levels of cyclins determining G2/M cell cycle arrest, and induced a canonic apoptotic pathway.	Emanuele et al., 2017
5	Brucea javanica	Quassinoids, Brusatol.	Hepatoma 22 (H22) cells in Ascitic tumor bearing mice (in vivo)	1. Suppressed the growth of hepatoma H22 cells in mice. 2. Induced apoptosis in the H22 cells.	Wang et al., 2021
6	Lepidium sativum	Flavonoids, Glycosides, Polyketides, Linolenic, Oleic acid, Monoterpenes, Methyleugenol, Sesquiterpenes, Caryophyllene.	HuH-7, HepG2 cells (in vitro)	1. Showed significant increases in the mRNA transcripts of P53 and BAX genes in both the HuH-7 and HepG2 cell lines.	Nazir et al., 2021

Table 5:- Phytochemicals and their bioactive components from flower of plants.

Sl. No	Plant	Active Compounds	Cell line or animal used for testing	Result	Author and Year
1	Spilanthes paniculata	Phenols, Flavonoids. N -isobutylamide	Huh-7 cells (in vitro)	1. Showed anti-proliferative effect by induction of caspase-3	Mishra et al., 2015

		Spilanthol.		enzymes. 2. Inhibition of phosphorylation of tyrosine kinases. 2. Degradation of DNA of Huh-7 cells were also found.	
2	Allium atroviolaceum	Sapogenin (atroviolacegenin), Saponins.	HepG2 cells (in vitro)	1. The decreased expression of anti-apoptotic protein (Bcl-2). 2. Apoptosis occured via., sub G0 cell cycle arrest. 3. Cytotoxic as well as anti-proliferative effect showed against HepG2 cells.	Khazaei et al., 2017
3	Prunus spinosa	Flavonoids, Phenol, Proanthocyanidins, Phenolic acid, Cyanogenic glycoside.	Hepa 1-6, AML 12 cells (in vitro)	1. Induced cell death primarily via., necrosis. 2. Percentage of dead cells increased in sample compared to the controls. 3. Hydrogen cyanide released from cyanogenic glycoside, can cause cell death by arresting ATP production and blocking cytochrome oxidase.	Murati et al., 2019
4	Cynara scolymus	Polyphenols, Cynarin, Caffeoylquinic, Chlorogenic acid. Flavonoids- Luteolin, Sesquiterpenes (Grosheimin, Cyanoropicrin), Saponins.	Thioacetamide (TAA) induced HCC in albino rat (in vivo)	1. Reduced the elevation in liver enzymes and oxidative stress. 2. Induced apoptosis by inhibition of metalloproteinase 3. Increase in the level of AFP in HCC rats.	El-Mesallamy et al., 2020

Table 6:- Phytochemicals and their bioactive components from flower stigma of plants.

Sl. No	Plant	Active Compounds	Cell line or animal used for testing	Result	Author and Year
1	Crocus sativus	Crocin, Crocetin, Carotene, Safranal.	DEN-induced liver cancer in rat (in vivo), HepG2 cells (in vitro)	1. Reversed the DEN-induced increase in the number and incidence of hepatic dyschromatic nodules. 2. Exhibited chemo-preventive effect against liver cancer by inhibiting cell proliferation and induction of apoptosis. 3. Modulate oxidative damage and suppression in inflammatory response.	Amin et al., 2011

Table 7:- Phytochemicals and their bioactive components from aerial parts of plants.

Sl. No	Plant	Active Compounds	Cell line or animal used for testing	Result	Author and Year
1	Phyllanthus amarus	Alkaloids, Tannins, Gallocatechins, Geraniin, Hypophyllanthin, Niranthin, Phyllanthin, Quercetin, Saponins.	N-nitrosodiethyl-amine (NDEA) induced Heptoma in Wistar rat (in vivo)	1. Increased the survival days of diseased testing animals. 2. Extract possess DNA polymerase enzyme of hepatitis B virus.	Rajeshkumar and Kuttan, (2000)
2	Enicostemma littorale	Flavanoids (Apigenin, Genkwanin), Glycoside, Alkaloid Enicoflavin, Catechin, Betulin, Terpines, Saponins.	p -DAB Induced HCC in Rats (in vivo)	1. Restoredthe functions of liver affected with carcinogens. 2. Increased the activity of glutathione and acted as scavenger to prevent damage due to free radicals. 3. Prevented lipid per-oxidation.	Gopal and Udayakumar, (2008)
3	Bacopa monnieri	Bacoside A.	DEN-induced and NDEA induced HCC in rats (in vivo)	1. Showed strong anti-oxidant and hepato-protective effects on carcinogens. 2. The extract decreased the activities of MMP-2 and MMP-9 thereby prevented tumor invasion and metastasis.	Janani et al., 2010; 2010
4	Mentha pulegium	Pulegone.	HepG2 cells (in vitro)	1. Showed remarkable concentration-dependent cytotoxicity of HepG2 cells.	Nikounezhad et al., 2014
5	Ochradenus Baccatus	Flavonoids, Quercetin, Glycosides Isoquercitrin, Quercitrin, Kaempferol Astragalin, Afzelin.	HepG2 cells (in vitro)	1. Modified mitochondrial pathway, thereby inducing apoptosis in HepG2 cells.	Bhatia et al., 2015
6	Origanum dayi	Cineole, Terpineol, Sabinene hydrate, Sabinene hydrate acetate, Terpinen, Linalyl acetate.	HepG2 cells (in vitro)	1. Induced cell death via., apoptosis through mitochondrial pathway. 2. Showed anti-proliferative effect in HepG2 cells.	Bhatia et al., 2015
7	Rumex vesicarius	Flavonoids, Quercetin, Myricetin, Anthraquinons, Carotenoids.	NDEA induced HCC in Wistar rats. (in vivo)	1. Reduced activities of liver enzymes like ST, ALT, ALP, GPC3 in serum. 2. The extract promoted apoptosis, stimulated inhibition of proliferation of cells and showed antioxidant activity.	Shahat et al., 2015
8	Veronica ciliate	Iridoid compounds,	HepG2 cells	1. Reduced proliferation of HepG2	Yin et al., 2016

		Veronicoside, Catalposide, Amphicoside, Verminoside.	(in vitro)	cell in a dose-dependent manner. 2. Extract exhibited antioxidant activities and DPPH radical scavenging. 3. Showed protective effects against acute hepato-toxicity induced by CCl_4.	
9	Kochia indica	Phenolic compound, Phenyl hexachloro tetra hydroxy heptane.	HepG2 cells (in vitro)	1. Extract enhanced the cytotoxicity of cells as a concentration dependent manner. 2. The cell viability of HepG2 was gradually decreased with increasing concentration of the plant extract.	Abdel-Hamid et al., 2017
10	Origanum vulgare	Carvacrol, Thymol, Citral, Linalool, Sesquiterpenes, Monoterpenes, Limonene.	HepG2 cells (in vitro)	1. Induction of cell death by apoptosis or necrosis, which increased cell permeability and loose cytoplasmic organelles. 2. Extract exhibited a lipophilic nature, interfered with membrane-catalyzed enzymes and enzymes in energy and protein production causing cell death.	Elshafie et al., 2017
11	Veronica sibirica	Sibiriquinone A, Cryptotanshinone, Tanshinone I and II, Diterpenes.	BEL-7402 cells (in vitro)	1. Showed cytotoxic activity against BEL-7402 cells. 2. Inhibited BEL-7402 cells proliferation and growth.	Salehi et al., 2019
12	Nepeta baytopii	Luteolin, Apigenin, β-caryophyllene, Germacrene-D, Cineole, Pinene. Fertaric acid, Hydroxycinnamic acid, Spathulenol.	HepG2 cells (in vitro)	1. The extract exhibited cytotoxicity against HepG2 cells. 2. Enzyme inhibitory and anti-oxidant properties were observed.	Zengin et al., 2021
13	Pulicaria aubertii	Triterpenes (Pseudotaraxaterol, Stigmasterol), α-tocospiro B. Flavonols, Hydroquinones.	HepG2 cells (in vitro)	1. Showed anti-diabetic and cytotoxic activities. 2. It possesses high anti-inflammatory effect.	Mohammed et al., 2021
14	Frankenia laevis	Phenolic acids, Lignans, Flavonoids, Monoterpenes, Linoleic acid.	HepG2 cells (in vitro)	1. Showed high cytotoxic effect on the human HCC (HepG2) cells. 2. Exhibited antioxidant activity, enzyme inhibition and cytotoxicity.	Rodrigues et al., 2022
15	Suaeda vermiculata	Octadecanoic, Palmitic, Elaidic, Linoleic acid, Kaempferol, Gingerol, Quercetin.	HepG2 (in vitro)	1. Extract possesses high binding affinity against ABC transporter family proteins and thus considered to be MDR proteins inhibitors.	Mohammed et al., 2022

				2. Improved the sensitivity of the DOX in HCC.	

Table 8:- Phytochemicals and their bioactive components from latex of plants.

Sl. No	Plant	Active Compounds	Cell line or animal used for testing	Result	Author and Year
1	Calotropis procera	Cardenolides.	X15-myc trans-genic mouse of Hepatoma (in vivo), Huh7, COS-1, AML12 cells (in vitro).	1. The extract showed protection against hepato-carcinogenesis in the mice. 2. Promoted extensive cell death in Huh-7 and COS-1 cells but the non-transformed hepatocytic(AML12) cells spared.	Choedon et al., 2006

Table 9:- Phytochemicals and their bioactive components from roots of plants.

Sl. No	Plants	Active Compounds	Cell line or animal used for testing	Result	Author and Year
1	Rehmannia Glutinosa	Polysaccharides, Polyphenols, Flavanoids.	Rat cells (H-4-II-E) (in vivo) HA22T/ VGH cells (in vitro)	1. Showed dose-dependent inhibition of proliferation of H-4-II-E cells. 2. Inhibited proliferation and stimulated p53-mediated apoptosis in HA22T/VGH cells.	Chao et al., 2006
2	Morinda Citrifolia	Anthraquinone, Damnacanthal.	HepG2 cells (in vitro)	1. Inhibition of growth and clonogenic potential of HepG2 cells, as well as induction of cell apoptosis. 2. Damnacanthal, the bioactive compound in the extract inhibited tyrosine kinase.	García-Vilas et al., 2015
3	Sclerocarya Birrea	Polyphenols, Flavonoids, Quercetin, Tannins.	HepG2 cells (in vitro)	1. The extract was able to enhance the intracellular reactive O2 species levels in cancer cells, thereby promoting cell death.	Armentano et al., 2015
4	Rauwolfia vomitoria	Alkaloids, Tannin, Saponins, Flavonoids, Steroids, Terpenoids, Cardiac glycosides.	HepG2 cells (in vitro)	1. Inhibited proliferation of HCC cells (HepG2).	Tekwu et al., 2017
5	Bergenia ciliate	Pyrogallol, Rutin, Morin.	DEN induced HCC in Balb C mice (in vivo)	1. Enhanced albumin levels with decrease in the levels of tumor markers AST, ALT, LDH, AFP etc., and bilirubin. 2. It exhibited cytotoxic effects and have apoptotic properties against HCC in vivo.	Dar et al., 2019
6	Glossostemon bruguieri	Flavonoids, Apigenin, Terpenoid, Squalene. Glycoside	HepG2, Hep3B cells (in vitro)	1. Stimulated growth-inhibitory effects against HCC cells, but showed no cytotoxic effect on normal hepatocyte.	Al-Snafi, 2019

		Isoscutellarein. Lipids, Octacosane.		2. Induced apoptotic effects to HepG2 cells in a caspase-dependent manner and via., up-regulating p53/p21.	
7	Persea americana	Oleic acid, Palmitic acid.	HepG2 cells (in vitro)	1. The extract affected cell cycle arrest, retarded development and activated apoptosis. 2. Showed significant inhibition of HCC.	Alkhalaf et al., 2019
8	Curcuma longa	Curcuminoids, Curcumin, Dimethoxy, Bisdemethoxycurcumin, Sesquiterpenoids.	HepG2 cells (in vitro), Swiss albino rats with CCl 4 induced hepatotoxicity (in vivo)	1. Showed suppression of angiogenic cytokines, which inhibit angiogenesis in certain tumors. 2. Induced apoptosis via., p53-dependent pathway. 3. Inhibition of pro-inflammatory transcription factors.	Gull et al., 2022

Table 10:- Phytochemicals and their bioactive components derived from stem and bark of plants.

Sl. No	Plant	Isolated Bioactive Compounds	Cell line used for testing	Result	Author and Year
1	Senecio latifolius	Pyrrolizidine, Retrorsine.	HuH-7 cells (in vitro)	1. The extract promoted effects like micronuclei or apoptosis or abnormal multinucleate cells in HuH-7 hepatoma cells. 2. Exhibited aberrant spindle formation in dividing cells. 3. Showed some improper intracellular architecture like re-arranged cytoplasmic tubulin.	Steenkamp et al., 2001
2	Terminalia arjuna	Tannins, Polyphenols (Flavonols, Flavones, Phenyl propanoids).	DEN induced HCC in rats (in vivo)	1. Observed high level of lipid peroxidases. 2. The levels of enzymatic and non-enzymatic antioxidants reduced. 3. The enzyme levels changed significantly.	Jain et al., 2009
3	Tinospora cordifolia	Epoxy clerodane, Diterpene.	DEN induced HCC in rats (in vivo)	1. Reduced level of tumor incidence and damaged hepatocytes reversed to normal. 2. Exhibited preventive effect against chemically induced HCC in rats.	Dhanasekaran et al., 2009
4	Symplocos racemosa	Triterpenoids, Betulin, Amyrin, Oleanoic acid, Flavonoids, Phenolic glycoside	DBMA induced HCC in Wistar rats (in vivo)	1. Exhibited hepato-protective effect by reducing activities of the serum enzymes like ALP, TB, DB, SGOT, SGPT etc.	Vijayabaskaran et al., 2010

		salireposide, Sitosterol.		2. Reduced lipid peroxidation, glutathion, catalase levels and increased proteins in a dose-dependent manner.	
5	Pinus massoniana	Proanthocyanidin.	HepG2 cells (in vitro), Kunming mice (in vivo)	1. Induced apoptosis in human hepatoma cells, through caspase-dependent pathways. 2. PMBE inhibited cell viability in a dose- and time-dependent manner in HepG2 cells.	Ma et al., 2010
6	Cochlospermum angolensis	Phenolics, Flavonoids.	HepG2 cells (in vitro)	1. Possesses antioxidant activity and as well as anti-hepato-cellular carcinoma activity.	Pereira et al., 2013
7	Ferula communis	Coumarin derivative – Umbelliferone.	HepG2 cells (in vitro)	1. Umbelliferone treatment induced cell cycle arrest at S phase in HepG2 cells in a concentration-dependent manner. 2. Stimulated a dose- and time-dependent reduction in cell viability and DNA fragmentation.	Yu et al., 2015
8	Rauwolfia vomitoria	Tannin, Saponins, Steroids, Flavonoids, Terpenoids, Cardiacglycosides.	HepG2 cells (in vitro)	1. The extract showed some inhibitory effects on the proliferation of HCC cells.	Tekwu et al., 2017
9	Chrysophyllum Cainito	Flavonoids (Quercetin, Catechin, Epicatechin, Gallocatechin, Gallic acid, Myricitrin), Phenols, Steroids, Saponin, Tannin.	HepG2 cells (in vitro)	1. Exhibited induction of apoptosis in Human HCC in HepG2 cells. 2. The extract reduced viability of HepG2 cells in a dose- dependent manner.	Doan et al., 2020

Table 11:- Phytochemicals and their bioactive components from whole parts of plants.

Sl. No	**Plant**	**Active Compounds**	**Cell line or animal used for testing**	**Result**	**Author and Year**
1	Andrographic paniculata	Andrographolide, Panaculoside, Flavonoids, Andrographonin, Panicalin, Apigenin.	HepG2 cells (in vitro)	1. Enhanced antioxidant and hepato protective activities. 2. Showed increased activities of enzymes like glutathione trasferase and glutamyltrans peptidase.	Trivedi et al., 2007
2	Piper sarmentosum	Amides, Flavonoids, Lignans, Terpenes, Steroids, Prophenyl, Phenols.	HepG2 cells (in vitro)	1. Promoted an intrinsic apoptosis pathway to induced anti-carcinogenic activity in HepG2 cells.	Zainal et al., 2009
3	Solanum nigrum	Gallic acid, Protocatechuic acid, Aallocatechin, Caffeicacid,	HepG2 cells (in vitro), rats with hepatotoxicity (in	1. Promoted inhibition of hepato-carcinoma cell growth by arresting cells at G2 /M phase.	Wang et al., 2011

		Gallocatechin Gallates, Rutin, Quercetin, Naringenin.	vivo)	2. Recorded decreased tumor weight and tumor volume in mice. 3. Stimulated cell death by means of apoptosis.	
4	Silybum marianum	Flavonoligans, Silymarin, Silibinin.	HepG2 cells (in vitro)	1. The extract showed extensive antioxidant properties.	Pereira et al., 2013
5	Fumaria indica	Flavanoids, Tannins, Glycoside, Alkaloid, Terpines, Saponins, Steroids.	HCC in Wistar albino rats and Swiss albino mice (in vivo)	1. The extract showed regression of tumours in liver. 2. Promoted restoration of the activities of liver cancer marker enzymes. 3. Reduction in lipid peroxi-dation (LPO) and increase in the antioxidant enzymes. 4. PreventedNDEA-induced hepato carcinogenesis.	Aziz et al., 2019
6	Luffa cylindrical	Flavonoids, Phenolics, Oleanolic acid, Tocopherol, Carotenoids, Triterpenoids.	Circulating cancer stem cells in human HCC grade II and III (in vitro)	1. Possessed cytotoxic activity against circulating tumor cells of HCC. 2. The level of cancer stem cells in blood of HCC patients seem to be decreased.	Abdel-Salam et al., 2019
7	Fructus aurantii	Flavonoids, Eriocitrin, Narirutin, Naringin, Hesperidin, Meranzin, Nobiletin, Tangeretin.	HepG2 cells (in vitro)	1. Showed inhibition of HepG2 cells proliferation. 2. Flavonoids decreased the level of glycolysis rate limiting enzymes gene expression in HepG2 cells.	Luo et al., 2022

Discussion:-

According to the examination of the aforementioned studies, the principal phytochemical substances that were discovered are essentially various types of alkaloids and polyphenols like flavonoids. They are the main components having therapeutic qualities, notably anticancer activities. There have been discoveries of some common compounds like Terpenoids, Catechins, Carotinoids, Coumarins, Anthocyanins, Quercetins, Oleanolic Acid, Quinones, Pyridines, Apigenins, and other significant bioactive compounds. These compounds are derivatives of alkaloids and flavonoids. Some phytochemicals, including Silibinin, Naringenin, Andrographonin, Panicalin, Diosgenin, Aloin, Emodin, and Cucurbitans etc.,were also be found depending on the therapeutic characteristics of each plant. Thus they support the disease's treatment or prevention in some or other way. The following are some of the results that the medicinal substances produced in the experiments conducted by the aforementioned researchers:

a. Prevents hepatoma cells from proliferation and being viable.
b. Encourages cancer cell death through necrosis or apoptosis.
c. Reduces the peroxidation of lipids.
d. Raises the level of antioxidant enzymes.
e. Treat and reverse the hepatoma caused by carcinogens like DEN (Diethylnitrosamine), NDEA (N-nitrosodiethylamine), p-DAB etc.
f. Induce DNA fragmentation and suppress inflammatory damage to the liver.
g. Enhances the reactive oxygen species (ROS) within cells.
h. Lower the concentrations of tumour markers and lot more.

Figure 1:- Data of research included in this review done from the year of 2000 to 2022.

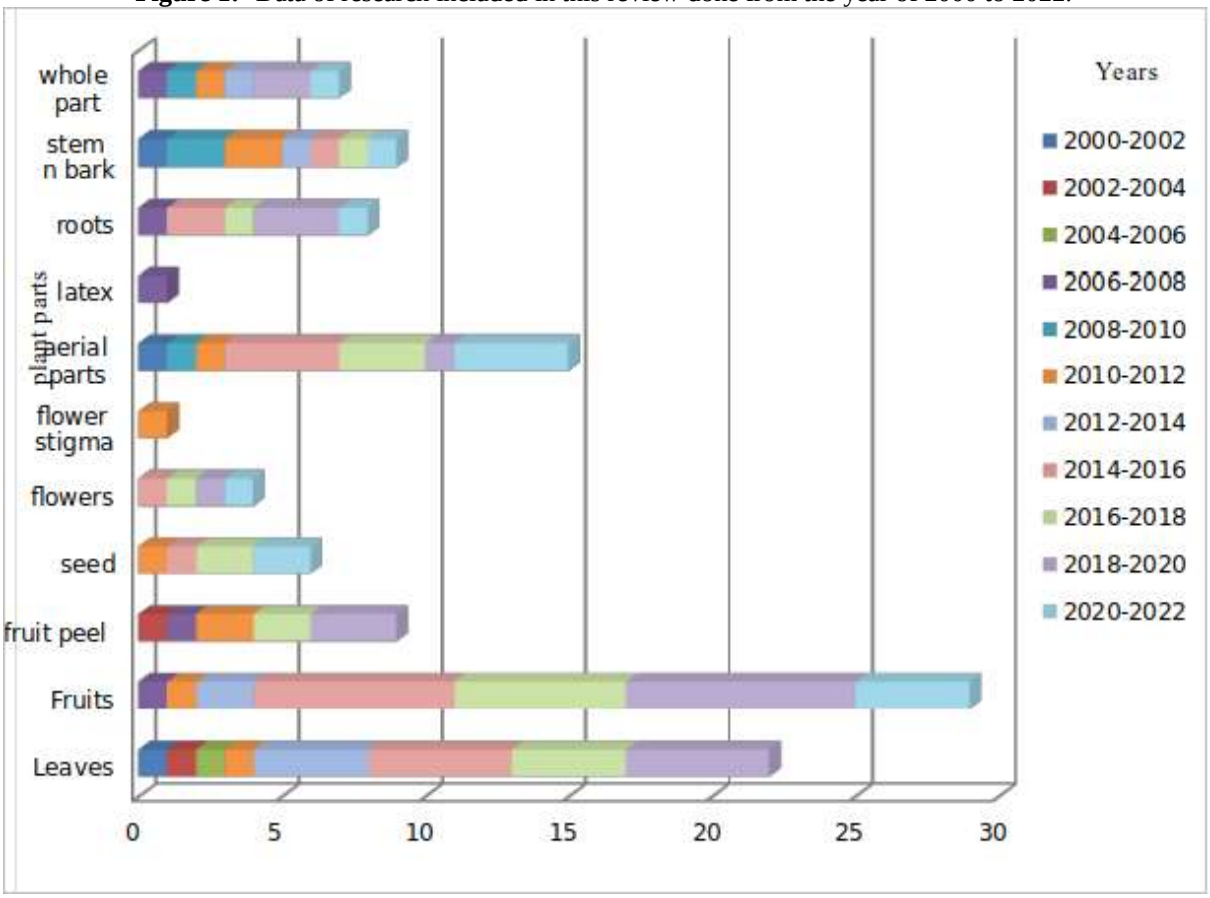
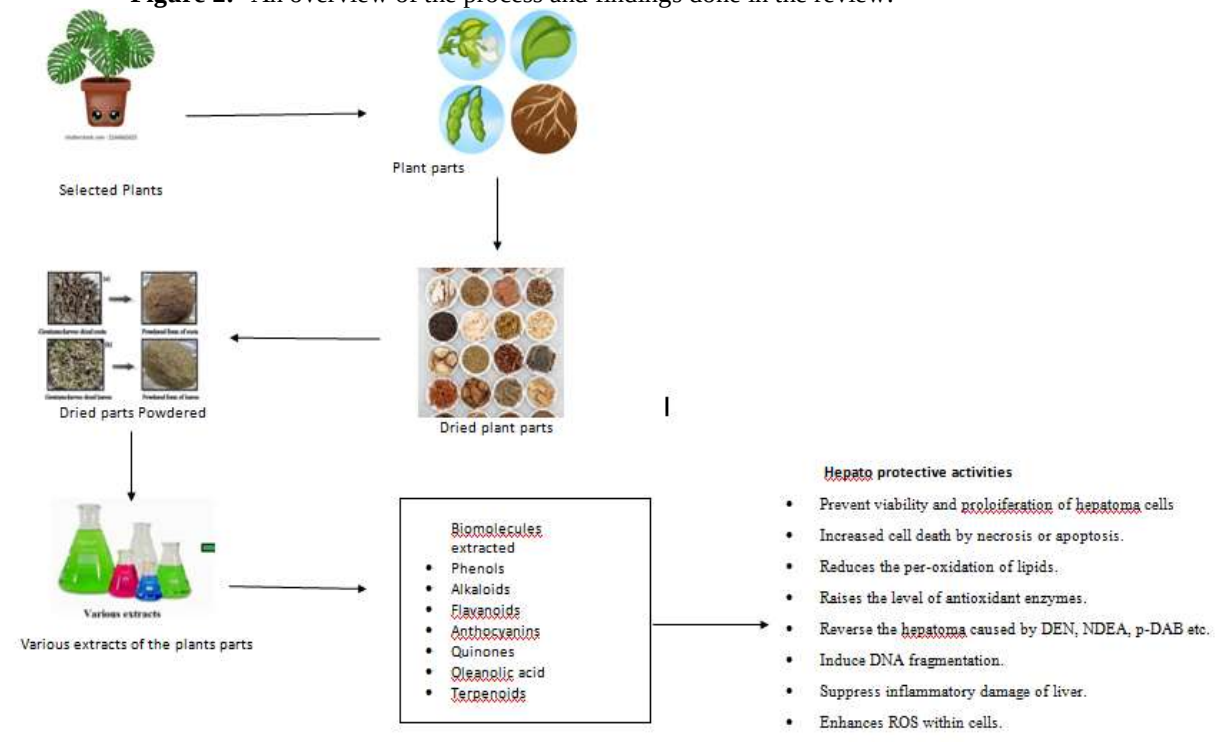


Figure 2:- An overview of the process and findings done in the review.



Secondary metabolites and their derivatives have been shown to be the main biochemical substances involved in the treatment and prevention of hepatocellular cancer. In treating cancer cells, they are efficient and secure, and can therefore be employed to treat patients as modified drugs.

Conclusion:-

This review shows the availability of bioactive compounds from the pool of natural resources. Only two decades worth of research served as the foundation for this study. However, both the plants selected for the study and the phytochemicals found are more numerous. It appears that secondary metabolites and their derivatives make up the majority of phytochemicals. There are other more substances also have been found to be effective against the disorders. As a result, it is certain that there will be opportunities to find a lot more phytochemicals in the untried and unidentified plants that Mother Nature has provided. To discover a far more potent, long-lasting, appropriate, and secure treatment for the dreaded and deadly HCC, additional research and tests should be carried out in this area. For the effective treatment of the disease, techniques for using these chemotherapeutic medicines should also be developed through additional research and study.

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