

Anti-Cancer Properties of Flavonoid Phyto Compounds: A Brief Review

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Cancer is one of the leading causes of death. There are a variety of therapies used to manage cancer cells, such as hormone therapy, radiation, chemotherapy, and surgery. Nonetheless, there are numerous adverse effects of these treatments. In this regard, the necessity to find an alternative treatment in the cure of the cancer cells emerges. In this line, natural chemicals derived from are required in such circumstances. Scientists across the globe are discovering that natural phytochemicals of plant sources are useful in the treatment of different types of cancers. This review provides a summary of the modern biomedical and pharmacological results on the anticancer effects of flavonoids, their mechanisms of action, and therapeutic implications. There is a large body of in vitro and in vivo literature suggesting that flavonoids, including quercetin, apigenin, luteolin, kaempferol, and catechins, inhibit tumor cell proliferation, induce apoptosis, arrest the cell cycle, and inhibit angiogenesis and metastasis. The review demonstrates that flavonoid phytochemicals have therapeutic potential and are promising candidates in the field of cancer prevention and adjuvant therapy, but more pharmacokinetic and clinical research is required to confirm their efficacy and safety.

Keywords: Anticancer; Cancer; Flavonoid; Good Health; Natural anticancer properties; Phyto-compounds.

The cancer cell characterized by abnormal behavior and uncontrolled proliferation of the cells. There are more than 200 distinct forms of cancer, with symptoms and signs varying according to the type, size, location, and stage of the disease.^{1,2} Biopsy may be of vital importance in terms of the nature of the abnormal tissue as well as the detection of the precancerous alterations as well as the actual type of cancer and its stage of development in case it occurs. The methods of treatment vary according to the tumour's kind and dimensions.³ The predominant conventional therapies for cancer

encompass radiation, chemotherapy, and surgical intervention. Moreover, herbal therapy constitutes one of numerous alternative and complementary modalities for cancer treatment.⁴ Chemotherapy possesses considerable potential to diminish the incidence of cancer. Chemo preservation uses many techniques to inhibit, postpone, or regulate the proliferation and dissemination of cancer. Research on chemo preservation has significantly intensified due to the identification of potent molecular targets that can impede carcinogenesis, along with breakthroughs in our comprehension

of the carcinogenic process.⁵ Annually, well over 11 million individuals globally receive a cancer diagnosis, with 6.7 million tragically succumbing to the illness. The most commonly diagnosed cancers worldwide are breast, lung, and colorectal cancers, although lung, stomach, and liver tumours demonstrate the highest fatality rates. Due to the obstacles posed by contemporary cancer therapies, including insufficient efficacy, heightened sickness severity, higher death rates, and reduced quality of life during treatment, there is an urgent necessity for novel and alternative herbal approaches to manage and prevent the disease.^{6,7}

Traditionally, plants are one of the major sources of cure to a wide range of diseases. Ayurveda, Traditional Indian Medicine (TIM), and Traditional Chinese Medicine (TCM) are among the most ancient medicinal systems still in operation today, originating circa 4500 BC.⁴ Historically, oral traditions conveyed knowledge regarding the selection of suitable plants, the ideal periods for their harvest, and techniques for remedy preparation. The modern scientific evidence indicates that phytochemicals have a substantial ability to combat cancer. Remarkably, plants constituted the foundation for nearly 50% of all licensed anticancer medication.⁸⁻¹⁰ This review evaluates anti-cancer properties flavonoid phytochemicals.

MATERIALS AND METHODS

The literature review of the anticancer properties of different parts of plants was carried out based on various data on the Internet, on the databases of the World Health Organization, and a variety of scientific sources, including Web of Science, Taylor and Francis, PubMed, ResearchGate, Springer, Wiley, Google scholar and the National Cancer Institute database. The search through the use of the right search phrases identified studies published between 2010 and 2025, such as the use of the following search phrases, cancer, phytochemicals, pharmacological potential, and anticancer efficacy.

Phyto-compounds have natural anticancer activity

Secondary metabolites occur naturally in the entire plant, including its roots, stems, bark, leaves, flowers, fruits, and seeds, and are crucial

in plant defence and adaptation. Most of these metabolites play a role in the human health as they serve as therapeutic agents. They are very broadly divided into various large groups, including flavonoids, alkaloids, terpenoids, and phenolic acids, each of which is represented by different structures and action mechanisms. Together, these compounds exhibit a variety of biological effects, including antioxidant, anti-inflammatory, and antimicrobial properties, which have a considerable beneficial impact on human health.^{11,12}

There is growing data to suggest that phytochemicals also have significant anticancer effects. All these effects are mediated via several cellular mechanisms, which encompass induction of apoptosis, inhibition of cell proliferation, angiogenesis inhibition and regulation of tumour growth and metastasis signalling pathways. Moreover, a wide range of phytocompounds have selective cytotoxicity with respect to cancer cells but lack the cytotoxicity to normal healthy cells, which have possible benefits compared to traditional chemotherapeutic agents. Consequently, it is noted that secondary metabolites found in plant materials are progressively being considered as viable prospects in cancer preventive and therapeutic applications.¹³

Phenolic Compounds

Phenolic compounds are a class of phytochemicals characterized by the presence of one or more phenol units containing hydroxyl (-OH) groups and are richly distributed in nature. Based on their structural complexity, they are considered into several subclasses, including flavonoids, phenolic acids, tannins, stilbenes, and lignans. Each group exhibits distinct biological activities and plays a crucial role in plant physiology, such as providing antioxidant, anti-cancer, anti-microbial, and anti-inflammatory effects and protecting against ultraviolet radiation. The wide range of functional properties of phenolic compounds contributes significantly to the health benefits derived from consuming fruits, vegetables, and other plant-based foods rich in these bioactive molecules.¹⁴⁻¹⁶

Flavonoids

Flavonoids are the largest group of phenolic compounds; these polyphenolic compounds are found abundantly in fruits, vegetables, tea, and wine. Flavonoids have strong abilities to fight

against oxidation, reduce inflammation, and prevent tumours, with examples including quercetin, catechins, and genistein.¹⁷ Polyphenolic substances known as flavonoids include flavones, flavanones, isoflavones, flavonols, chalcones, flavanols, and anthocyanins, each possessing unique structures and health benefits. Research has shown that regular consumption of flavonoid-rich foods may contribute to a lower risk of chronic diseases, such as cardiovascular conditions and certain types of cancer, highlighting their importance in a balanced diet.¹⁸

In this review, twenty-four bioactive compounds, derived from twenty plant species belonging to thirteen botanical families, were analyzed shown in Table.1. All the investigated plants exhibited notable anticancer properties. These results highlight the promising potential of natural products as sources for the development of novel cancer therapeutics.

Apigenin is a non-mutagenic flavonoid that is abundant in various plants and fruits, including parsley, onions, wheat sprouts, chamomile, seasonings, tea, and citrus. It can prevent the development of malignancy. Apigenin has been demonstrated to function through several mechanisms, such as the suppression of signal transmission, prevention of mutagenesis, and stimulation of cell cycle arrest and death. The most promising drug for treating the growth arrest of colorectal cancer cells was apigenin (flavone), which was developed using the finest flavonoids for cell growth inhibition.¹⁹

The milk thistle extract was investigated for anticancer research, particularly for its potential application in treating colon cancer cells, including LoVo and multidrug-resistant isogenic LoVo/DX, which are chemoresistant tumours. Silymarin inhibited both cell lines' proliferation. Low silymarin pre-treatment synergised with doxorubicin and paclitaxel in LoVo but not LoVo/DX. Higher silymarin concentrations were added to doxorubicin and paclitaxel in both cell lines. Silymarin improved chemotherapeutic absorption and cell cycle effects in LoVo but not LoVo/DX. These findings show that silymarin can treat colon cancer, including multidrug-resistant forms, at high yet therapeutically attainable dosages. Due to its low toxicity, two regimens using low- and

high-dose silymarin pre-treatment may be useful for combination therapy.²⁰

It was established in the study that silibinin and metformin in combination were more effective at inhibiting the proliferation of the human colon cancer cell line (COLO 205 cell line). The combination of 100 $\mu\text{mol/L}$ silibinin and 10 $\mu\text{mol/L}$ metformin worked better than the mix of 50 $\mu\text{mol/L}$ silibinin and 5 $\mu\text{mol/L}$ metformin, and it did not damage the HCoEpiC cells (Human Colonic Epithelial Cells), which are normal human colon epithelial cells, hence its selective anticancer effect. This is indicative of a potential therapeutic approach to colorectal cancer that can be used on the cancer cells and cause little harm to the normal tissue, which can eventually lead to fewer adverse side effects as compared to traditional chemotherapy.²¹

Curcumin is a natural polyphenolic substance that is produced using *Curcuma longa* (turmeric). It has been broadly researched due to anticancer effects against various types of cancers such as breast, colon, lung, prostate, liver, cervical, and skin cancers. Curcumin has decreased the humanity of glioma cell line. One time concentration of 25 and 50 $\mu\text{mol/L}$ was added in cell seeded plate. Curcumin has cytotoxicity in glioma cells and viability of 25 $\mu\text{M/L}$ and 50 $\mu\text{M/L}$ at 490nm gave 68 and 27 percent in ELISA plate reader respectively. The level of cytotoxicity on glioma cell is high in this concentration of 50 $\mu\text{M/L}$. The anti-cancer activity of curcumin in U87MG glioma cell was demonstrated and that is possibility curcumin regulate the cellular signalling pathway of the toxicity in GBM cells.²²

Similarly, curcumin has demonstrated to possess an extensive range of therapeutic effects including anti-inflammatory, chemo-preventive, anti-proliferative and anti-metastatic. The review will give an insight on the recent studies that have been done to address the issues with bioavailability of curcumin, preclinical and clinical trials that have reported success in combinatorial approaches that couple curcumin with other treatments. Studies on signaling pathways that curcumin treatment can affect reveal that it is a highly potent agent of canonical intracellular components that are related to the major processes such as genomic modulations, cell invasion and cell death signalling.

Table 1. Reported anticancer flavonoids Phyto-compounds of various plant sources

S. No	Plant species	Phytocompound (s)	Doses	Cell line	References
1.	<i>Artemisia argyi</i>	Artemisinin	1.11 μ M 2.13 μ M 25.62 μ M	HL-60 HT-29 A549	47
2.	<i>Sylbium marianum</i>	Silymarin	1.03 $\pm$ 0.04	LoVo and LoVo/DX	20
3.	<i>Sylbium marianum</i>	Silibinin	50 μ mol/L	COLO 205 (HCoEpiC)	21
4.	<i>Glycyrrhizauralensis</i>	Isoliquiritigenin	NA	NCI-H1975, HCC827GR and A549)	48
5.	<i>Bauhinia variegata</i>	Kaempferol	6 μ g/mL	EC9706	25
6.	<i>Psoralea corylifolia</i>	Psoralidin	Not report	PC3	49
7.	<i>Ginkgo biloba</i>	Ginkgetin	Not report	MG-63, SAOS-2, and U-2 OS	50
8.	<i>Ocimum sanctum</i>	Quercetin	LD50 = 87.74	A549	51
9.	<i>Scutellaria baicalensis</i>	Orientin	Not report	oral carcinoma (KB) cell lines	52
10.	<i>Rumex japonicus</i>	Vicenin	Not report	oral carcinoma (KB) cell lines	53
11.	<i>Capsicum annuum</i>	Baicalenin	Not report	A549	54
12.	<i>Camellia sinensis</i>	Quercetin	23.8 μ M	HepG2	55
13.	<i>Camellia sinensis</i>	Luteolin	Not report	HCT-116	49
14.	<i>Vitis vinifera</i>	Epigallocatechin gallate	Not report	B19	56
15.	<i>Curcuma longa</i>	Epigallocatechin gallate	9 μ g/mL	SGC-7901	57
16.	<i>Alpinia galangal</i>	Procyanidin	Not report	MCF-7 and BT-47 cells	58
17.	<i>Curcuma longa</i>	Curcumin	Not report	HCT-116	59
18.	<i>Curcuma longa</i>	Curcumin	CUC-1, 300 mg solution, once per week	PANC-1, MIA PaCa-2, and AsPC-1	60
19.	<i>Curcuma longa</i>	Curcumin	32.5 μ g/mL	4TI cell line	54
20.	<i>Curcuma longa</i>	Curcumin	Not report	SGC-7901	61
21.	<i>Zingiber officinale</i>	Curcumin	97mg/mL	HeLa cells	62
22.	<i>Hippophae rhamnoides</i>	Isorhamnetin	Not report	HT 29, HCT116 and SW480	30
23.	<i>Hippophae rhamnoides</i>	Isorhamnetin	25 μ M	A-549 lung cancer cells	

Curcumin is a possible compound in preventing and treating cancer.²³

Rahman et al.²⁴ evaluate the in vitro anti-proliferative properties of n-hexane, aqueous, ethyl acetate, methanol, tamoxifen, and ethyl acetate extracts of *Annona* against breast cancer cell lines MCF7 and MDA-MB-231. The results indicate that the aqueous extract efficiently suppresses breast cancer cells, specifically MCF7 (LD_{50} =23 mg/mL), while the n-hexane extracts regulate the MDA-MB-231 cell line (LD_{50} =24 mg/mL).²⁴ The human esophageal cancer cell line EC9706 was used to test kaempferol's anticancer properties. The results of the MTT assay indicate that kaempferol has a cytotoxic effect.²⁵

According to Ademiluyi et al.,²⁶ procyanidin has shown anticancer effects via several pathways, which include inhibition of pro-inflammatory cytokine, the phosphoinositide 3-kinase/protein kinase B /mammalian target of rapamycin (PI3K/AKT/mTOR) and mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) pathways and modulation of apoptotic proteins, including BCL2-associated X protein. Recent studies have identified several new delivery systems, including nanoparticles and liposomes to improve systemic absorption and therapeutic effectiveness. Clinical trials are ongoing to examine the possibility of procyanidin to be used as adjuvants in cancer treatment either by itself or combined with chemotherapeutic agents. Further research is needed to perfect their pharmacokinetics, have synergies with current treatments, and large-scale clinical trials can be used to prevent the possibility that the new agents are not effective and safe. PCs have the potential of being natural anticancer agents and complementing the conventional therapies and enhancing patient outcomes.

Spatholobus suberectus was prepared into ten procyanidin fractions of varying degrees of polymerization. The first time, trimers up to 11-mers were identified in *S. suberectus* extracts and their structures were deciphered by thiolysis and ESI-MS and MALDI-TOF-MS studies. The findings concluded that the average degree of polymerization (mDP) of crude *S. suberectus* procyanidins was 5.2 and the weight distribution of the monomer and the oligomers (mDP of 1.0–5.7) was 70.4% and that of the polymers (mDP 6.211.8)

was 25.6%. Catechin and epicatechin were the predominant monomeric units and small amounts of epigallocatechin and galocatechin were present. Interflavan linkages that were observed were A-type (minor type) and B-type (major type). The fractions that were highly enriched with the monomer and oligomers had the highest activities such as antioxidant activity and inhibitory activity on the growth of MCF-7 breast cancer cells as well as the lactate dehydrogenase A (LDH-A). Such findings also indicated that monomeric and oligomeric procyanidin fractions of SS might be further developed to become a useful source of antioxidants, LDH-A inhibitors, and possible breast cancer inhibitors.²⁷

Zhang et al.,²⁸ investigate the effects of licochalcone A on bladder carcinoma cell line UM-UC-3, J82 and HT-1197. The result finds that licochalcone A has proficient antiproliferative effects by blocking ERK1/2 mediated signaling cascades, thereby disrupting key processes required for tumor cell growth.

The bioactivity profiles of phenolic compounds isolated from black walnut kernels, the phenolic constituents were assessed to anticancer properties of tumorigenic alveolar epithelial cells (A549) and non-tumorigenic lung fibroblast cells (MRC-5). Among the 16 phenolic compounds examined, several-including penta-O-galloyl- α -D-glucose, epicatechin gallate, quercetin, (–)-epicatechin, rutin, quercetin 3- α -D-glucoside, gallic acid, (+)-catechin, ferulic acid, and syringic acid-demonstrated antioxidant capacities significantly greater than that of Trolox, the reference standard. Notably, penta-O-galloyl- α -D-glucose and quercetin 3- α -D-glucoside showed pronounced antiproliferative effects against both A549 and MRC-5 cells. These results suggest that the penta-O-galloyl- α -D-glucose emerging as a particularly strong candidate for use in pharmaceutical applications.²⁹

Evaluate the anticancer potentiating impact of isorhamnetin in conjunction with cisplatin and carboplatin; A-549 cells were subjected to treatment with isorhamnetin, cisplatin, and carboplatin. The findings indicated that the combination of isorhamnetin with cisplatin and carboplatin was more effective in reducing cancer cell proliferation and inducing apoptosis than single-agent treatment. The findings the

investigation indicate that isorhamnetin in conjunction with cisplatin and carboplatin may represent a viable clinical chemotherapeutic strategy for non-small cell lung cancer.³⁰

Martins et al.,³¹ investigates, the biochemical chrysin how to act as anticancer agent against the human colon adenocarcinoma model HT-29. Mechanistic studies revealed that the complexes induce apoptosis in cancer cells by impairing the functioning of mitochondria, the production of reactive oxygen species (ROS), and the promotion of the activities of caspase enzymes, thus clarifying the molecular mechanisms of their anticancer action. Overall, the findings highlight oxidovanadium (IV)-flavonoid complexes as promising chemotherapeutic candidates targeting redox-mediated apoptotic pathways in colorectal cancer, offering a potential strategy for designing metal-based anticancer agents derived from natural products.

The ethyl acetate extract of *Rumex japonicus* Hoult roots was assessed for cytotoxicity against HepG2, U251, and SK-OV-3/DDP cancer cell lines. Ten substances were obtained and characterised using NMR as emodin (1), chrysophanol (2), aloë-emodin (3), physcion (4), quercetin (5), resveratrol (6), β -sitosterol (7), 3 β -acetoxy-28-hydroxyurs-12-ene (8), sucrose (9), and one unidentified molecule. Compounds 1, 3, 4, 6, and 8 showed significant cytotoxicity ($p < 0.05$) against HepG2 cells; compounds 3–6 exhibited pronounced activity against U251 (IC₅₀ = 17.8–23.8 μ M); and compounds 1–6 revealed substantial cytotoxicity against SK-OV-3/DDP (IC₅₀ = 31.3–64.2 μ M). The results indicate that these compounds may hold potential as therapeutic agents in the treatment of various cancers, particularly those represented by the tested cell lines. Further investigation is warranted to elucidate their mechanisms of action and to assess their efficacy in vivo.³²

Galangin enhances TRAIL-induced apoptosis in human breast cancer cells by activating the AMPK signalling pathway. The combined treatment significantly increases apoptotic cell death compared to either agent alone, suggesting that galangin sensitizes breast cancer cells to TRAIL-mediated cytotoxicity. These findings highlight the potential of galangin as an adjuvant

therapeutic agent to improve TRAIL-based cancer therapy.³³

DISCUSSION

Bioactive secondary metabolites derived from plants, phytochemicals, have received considerable interest as anticancer agents because they are able to alter the activity of multiple cellular pathways.³⁴ These compounds have their effects realized in a number of mechanisms which are interrelated and this offers a reason why they should be used in cancer prevention and treatment.³⁵ Among the mechanisms is induction of apoptosis which is one of the major mechanisms that is dysregulated in cancer cells. There are numerous phytochemicals (flavonoids and alkaloids) that contribute to both intrinsic (mitochondrial) and extrinsic (death receptor-mediated) apoptotic mechanisms.³⁶ This includes the pro- and anti-apoptotic protein modulation, mitochondrion release cytochrome c and the caspases further activation which eventually leads to selective death of cancerous cells.³⁷

Moreover, phytochemicals have the ability to block the cell cycle thus preventing uncontrolled cell proliferation.³⁸ These compounds prevent the growth and replication of tumor cells by blocking cell division at key cells (G0/G1, S, or G2/M) by regulating cyclins, cyclin-dependent kinases (CDKs) and other checkpoint proteins.³⁹ Another important anticancer activity is angiogenesis inhibition. The development of a tumor needs new blood vessels to provide nutrients and oxygen. Phytochemicals have also been found to inhibit the vascular endothelial growth factor signaling and matrix metalloproteinases, which inhibit neovascularization and restrain tumor growth.⁴⁰

Moreover, a number of phytochemicals have been shown to have anti-metastatic activity because of the ability to regulate the epithelial-mesenchymal transition (EMT), adhesion molecules and extracellular matrix remodeling enzymes.^{41,42} Such effects minimise invasive and migratory potential of cancer cells restricting metastasis. Another mechanism is the modulation of oxidative stress which is a critical one. Normal cells use the antioxidant effects of phytochemicals, but

cancer cells, which are already in high oxidative stress, are further sensitized by pro-oxidant effect resulting in mitochondrial dysfunction, damage of DNA and apoptosis.⁴³ These diverse mechanisms, together, underscore the multi-targeted anticancer properties of phytochemicals, and prove them as good complementary or alternative cancer therapy. Their capacity to kill only cancerous cells and not normal cells is another factor that highlights their therapeutic potential and justifies further research on their clinical uses.⁴⁴⁻⁴⁶

Phyto-compounds as anticancer activity various phyto-compounds derived from different plant parts have been studied for their anticancer activity. In Table 1, artemisinin is the active compound found in *Artemisia annua*. It exhibited the highest activity against leukaemia and colon cancer cells, with mean GI50 values of 1.11 ± 0.56 μ M and 2.13 ± 0.74 μ M, respectively. The non-small cell lung cancer cell lines had the highest average GI50 value (25.62 ± 14.95 μ M), indicating they were the least responsive to ART in this test group. Intermediate GI50 values were acquired for melanoma, breast, ovarian, prostate, central nervous system, and kidney cancer cell lines. The result suggests that while artemisinin shows promise as a therapeutic agent against certain cancer types, its efficacy may be limited in others, particularly in non-small cell lung cancer. Further investigations are warranted to explore potential combinations or modifications to enhance its effectiveness across a broader spectrum of malignancies.⁴⁷

This review suggests that plant based natural compounds, as alternatives to synthetic chemicals, have demonstrated efficacy against cancer cells. Various plant phyto-compounds demonstrating anti-cancer effects have been documented in diverse investigations. Although there are still obstacles in transforming good research results into commercially viable medicines, further research, advancement in technology, and a team-based effort have a chance of achieving the potential of these natural chemicals in their use in the battle against cancer. The majority of researchers are concentrating on inhibit the cancer cells using phyto-compounds. Researchers note numerous failures due to difficulties in identifying active chemicals, insufficient characterisation, and challenges in comprehension. In the future, there

will be an increased emphasis on the production, growth, development, and application of natural anticancer characteristics to tackle diverse challenges. Further efforts in the manufacturing, formulation, and distribution of plant-derived active compounds are necessary to support the product's commercialisation. The investigation of biochemicals presents both challenges and prospects in the pursuit of effective cancer control. The endeavour to utilise these powerful molecules is laden with obstacles, including the identification of active constituents, their characterisation, and a thorough understanding of their actions. Nonetheless, the future holds promise as researchers redirect their attention to improving the creation and development of natural anticancer qualities. To actualise the complete potential of plant-derived active compounds, coordinated efforts in production, formulations, and delivery mechanisms are required. By surmounting these obstacles, we can facilitate the development of novel medicines that more effectively attack cancer and integrate easily into current therapy paradigms, providing promise for enhanced patient outcomes.

CONCLUSION

Flavonoids are a significant group of secondary metabolites produced by plants, and the significant anticancer effects of these types of secondary metabolites are based on the fact that they can alter various cells and affect molecular pathways. They act through causing apoptosis, cell cycle arrest, inhibition of angiogenesis and metastasis, regulation of oxidative stress, as well as epigenetic and immune changes. The non-selective cytotoxicity of flavonoids on cancer cells, combined with their comparatively low levels of toxicity in normal cells, demonstrates their potential to be safe and effective anticancer agents.

The next research would be to develop a systematic understanding of the pharmacokinetic, bioavailability, and molecular targets of flavonoids in vivo, since these parameters are vital in clinical translation. Increased stability and accumulation of nanoparticles or liposomal-based delivery systems might be developed, leading to increased therapeutic efficacy. Moreover, combining flavonoid-based with traditional chemotherapy or immunotherapy by means of a combinatoric

approach may generate synergistic anticancer effects with reduced side effects. Huge clinical studies are required to confirm the results of preclinical research and determine the standard dosing schedules, and in the future, provide the path to inclusion of flavonoid-based therapy into regular cancer treatment. In sum, flavonoids are a promising platform in designing new anticancer approaches either by themselves or as an adjunct to the conventional therapy.

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