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Effects of Polyphenols on ncRNAs in cancer - An update

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Abstract

In recent years, oncotherapy has received considerable attention concerning plant polyphenols. Increasing evidence suggests that due to the efficiency of polyphenols, they may have antitumor effects in various cancers. However, their regulatory structures remain elusive. Long non-coding RNAs (LncRNAs) have been identified in the regulation of various forms of tumorigenesis and tumor development. Long non-coding RNAs (LncRNAs) have recently emerged as regulatory eukaryotic transcripts and therapeutic targets with important and diverse functions in health and diseases. LncRNAs may be associated with the initiation, development, and progression of cancer. This review summarizes the research on the modulatory effects of LncRNAs and their roles in mediating cellular processes. The mechanisms of action of polyphenols underlying their therapeutic effects on cancers are also discussed. Based on our review, polyphenols might facilitate a significant epigenetic modification as part of their tissue-/cell-related biological effects. This finding may be attributed to their interaction with cellular signaling pathways involved in chronic diseases. Certain LncRNAs might be the target of specific polyphenols, and some critical signaling processes involved in the intervention of cancers might mediate the therapeutic roles of polyphenols.

Keywords: oncotherapy; polyphenols; LncRNAs; tumorigenesis; curcumin; EGCG; resveratrol

1. Introduction

Cancer growth is intimately linked to the unmanageable development of tumor cells. A worldwide focus has been drawn to cancer. Although conventional treatments like chemotherapy, surgery, and radiation therapy show great efficiency and benefits, drug interactions and toxicity remain in the majority of tissues in patients[1]. Effective antitumor factors need to be screened urgently in naturally existing resources and research strategies need to be improved. Dietary trends are closely linked to cancer incidence and growth[2]. Long non-coding RNAs (LncRNAs) are a class of RNA transcripts that are longer than 200 nt and have no obvious open reading frame [3,4]. They usually have structural features that are similar to those of mRNAs, such as 5′-cap structures and poly-A tails. Because of their low expression levels, lncRNAs were previously thought to be background "noise" produced by RNA polymerase II during transcription (i.e., no biological functions) [5,6]. Advances in lncRNA research revealed that most of the transcribed regions produce lncRNAs, which may have abundant functions [7,8]. Specifically, lncRNAs have important roles at the transcriptional [9], post-transcriptional [10] and epigenetic levels [11] via diverse regulatory mechanisms, including chromatin modification, transcriptional activation, transcriptional interference, and splicing regulation.

The LncRNAs have also been used for the selective killing of cancer cells [5,6]. During recent years, polyphenols derived from natural sources have demonstrated potential against LncRNAs [5,6]. The polyphenols are reported to be cost-effective with an ability to modulate multiple cell signaling pathways [7]. Moreover, these agents have been consumed for ages and, thus, are known to be safe [6-10]. The sources of polyphenols include fruits,

vegetables, spices, cereals, etc. The consumption of fruits and vegetables is associated with a reduced risk of chronic diseases [5,8]. Polyphenols can affect LncRNA expression either directly or indirectly through the involvement of miRNAs, protein kinases, enzymes, and transcription factors. In the cancer model, polyphenols can suppress the expression of oncogenic LncRNAs or can restore the functions of tumor suppressor LncRNAs [5-10]. The modulation of LncRNAs by polyphenols can produce therapeutic effects in some cancer types [6,7,9]. The disease models where polyphenols have been demonstrated to modulate LncRNAs include cancer, rheumatoid arthritis, osteoarthritis, and nonalcoholic fatty liver disease [6-10]. In disease models, polyphenols can both up-regulate and down-regulate LncRNAs [6,8,9]. The most common polyphenols known to have the potential to target LncRNAs include curcumin, resveratrol, EGCG, gambogic acid, and quercetin. Moreover, the modulation of LncRNAs by polyphenols can lead to the inhibition of survival, proliferation, migration, invasion, metastasis, and epithelial-to-mesenchymal transition [6-10]. The modulation of LncRNAs expression by polyphenols can also lead to chemo sensitization and radio sensitization of cancer cells. The effect of polyphenols on LncRNA expression in diverse diseases has been discussed in the following section. The positives and negatives associated with the targeting of LncRNAs by polyphenols are also discussed.

2. Polyphenols and their Biological Effects in Cancer

2.1. Classifications of Polyphenols

Plant metabolites are classified into primary or secondary metabolites depending on the functions they play in the plant system. While primary metabolites play an important roles in plants' growth and their survival[12], secondary metabolites are synthesized as

defense systems against disease and herbivores [13]. These secondary metabolites are bioactive compounds, which are very useful as functional foods [14]. Polyphenols are among the largest group of secondary metabolites found in plants [14]. Over 8000 structurally variants of polyphenols exist which are characterized by aromatic rings with one or more hydroxyl groups [15]. They are widely classified into classes and various subgroups based on the numbers of phenolic rings and structural elements attached to the rings [16]. The major classes are phenolics, flavonoids, stilbenes, and lignans[17]. Phenolic acids are sub classified into hydroxybenzoic acids including gallic acid or hydroxycinnamic acid and ferulic, coumaric, caffeic acid (represented in figure 1). The flavonoid subclass includes anthocyanidins, flavonols, flavanones, flavones, flavonols, and isoflavones.

2.2. Biological Roles of Polyphenols in Cancer

Clinical, epidemiological, preclinical studies have shown there is a strapping association connecting the polyphenols intake daily and défense from various forms of cancer [18-20]. Different trials show that polyphenol could be utilized for the anti-cancer effects via different biochemical signaling [21-25]. Dietary polyphenols exhibit effective anticancer efficacy via dynamic regulation of cell death pathways such as apoptosis and autophagy [26-28]. Moreover, to aid this context, these polyphenols mediate cell cycle arrest for inhibition of cell proliferation. Effective inhibition of invasion, metastasis, and angiogenesis by these dietary polyphenols have supported their chemotherapeutic efficacy [29]. In addition, dietary polyphenols orchestrate inhibition of inflammation-associated cancer initiation and progression [30,31].

2.2.1 EGCG

2.2.1.1. Role of EGCG

Tea catechins were first isolated by MichiyoTsujimura in 1929 in Japan [32] and since then four main types of catechins have been found in green tea leaves (-)-epigallocatechin-3-gallate (EGCG) accounts for approximately 59% of the total catechins from the leaves of the green tea, (-)-epigallocatechin (EGC) (19%), (-)-epicatechin-3-gallate (ECG) (13.6%), and (-)-epicatechin (EC) (6.4%) 33. The functional and structural differences between these catechinsare attributed to the number of hydroxyl groups on the B-ring and the presence or absence of a galloyl moiety [33]. EGCG induces apoptosis via Bcl2, Bax, BCL-XL, XIAP, and BAD (Usuwanthim et al. 2020).

2.2.1.2. Role of EGCG in different cancers

EGCG induced cell apoptosis through intrinsic mitochondrial pathway via activation of Caspase-9 in PC3 prostate cancer cells [34], MCF-7 breast cancer cells [35] and PANC-1, MIA-Pa-Ca-2, Hs 766 T, and AsPC-1 pancreatic cancer cells. EGCG has also been shown to induce apoptosis through the extrinsic death receptor pathway in MIA-Pa-Ca-2 pancreatic cancer cells via activation of Fas, DR5, and Caspase-8 [36]. In addition, EGCG downregulated the expression of anti-apoptotic proteins, such as BCL-2 in PANC-1[37], MIA-Pa-Ca-2, Hs 766 T, and AsPC-1 pancreatic cancer cells,[38] MDA-MB-231 breast cancer cells[39], NCI-H295 adrenal cancer cells [40] and PC-12 pheochromocytoma cells [41]. Moreover, EGCG induced apoptosis through both intrinsic and extrinsic pathways, regulatory proteins, and endoplasmic reticulum stress via activation of caspase-dependent, caspase-independent, death receptors, downregulation of anti-apoptotic proteins BCL-2, BCL-XL, and XIAP, and upregulation of pro-apoptotic BAD and BAX in NCI-H295 human adrenal cancer cells [38].

2.2.2. Curcumin

2.2.2.1. Role of curcumin

Curcumin (diferuloylmethane), polyphenolic dietary phytochemicals isolated from Curcuma longa acts as a strong antioxidant that provoked apoptotic cell death in numerous cancer cell lines [42]. It can induce apoptotic cell death via caspase 3, Bcl-2, and Bax/Bcl-2 expression [43]

2.2.2.2. Role of curcumin in different cancers

In human glioma (U-87MG) cells, curcumin induced apoptotic cell death through the regulation of caspase-3 and Bcl-2. In mesothelioma (MM-F1 and MM-B1) cell lines, curcumin treatment enhanced Bax/Bcl-2 expression 43. In addition to this, it cleaved PARP[43]. The activation of extracellular signal-regulated kinase1/2 (ERK1/2) expression and caspase 9 promoted apoptosis [44]. Moreover, curcumin enhanced the nuclear translocation of p53. In addition, it regulated the nuclear factor- κβ (NF-κβ)-dependent signaling pathways to induce apoptosis [45].

2.2.3. Resveratrol

2.2.2.1. Role of Resveratrol

Resveratrol (3,5,4-trihydroxystilbene), another dietary phytochemical. Similar to the other polyphenol it acts as a strong antioxidant, induces cell death via a different mechanism such as via reducing antioxidants and increasing oxidative stress via MDA and 8-OHdG [46].

2.2.2.2. Role of Resveratrol in different cancers

Resveratrol regulates extrinsic apoptosis through regulation of FAS-associated death domain (FADD) in leukemia cells [45]. Through regulation of Bax and Bcl-2, it also promoted intrinsic apoptosis [47]. In colon cancer cells, resveratrol induced reactive oxygen

species that further activated caspase-3 and caspase-8-dependent apoptosis [48]. Strong evidence indicated that Resveratrol declined hepatic carcinoma cell progression and oxidative damage and inflammatory cytokines regulated by Nrf2 in rats [49]. Kim and co-workers [50] indicated that Resveratrol caused mitochondrial biogenesis in Nrf2/ HO-1 activation in the HepG2 cells. Besides chemopreventive, antitumoral effects, Resveratrol enhanced the tumor cell's sensitivity to chemotherapeutic drugs. Li and co-workers [51] found that Resveratrol ameliorated the resistance to adriamycin (a chemotherapy drug) through regulation of the PI3K/Akt/Nrf2 activation in promyelocytic leukemia cells (HL-60). Cheng and co-workers [52] showed that Resveratrol ameliorated the response of pancreatic cancer cells to gemcitabine, enhancing the efficacy of gemcitabine in pancreatic cancer therapy. In the work, they indicated that this impact of Resveratrol was due to its ability to inhibit the nutrient-deprivation autophagy factor-1 (NAF-1) expression in pancreatic cancer cells through stimulating Nrf2 signaling. Resveratrol inhibited spleen dysplasia in broilers induced by high ambient temperature (HT) via stimulating the Nrf2 activating, thereby modulating oxidative stress indices (MDA, 8-OHdG, GSH, GPx, SOD, and CAT activities) and apoptotic indices (caspase-9, caspase-3, Bax, and Bcl-2) [46]. Resveratrol prevented mouse colon cancer induced by the azoxymethane (AOM) through Nrf2/HO-1 signaling leading to a decline in the iNOS, COX-2, and aldose reductase (AR) expressions and an increase in the activity of glutathione reductase (GSR) [53].

3. Classifications and Functions of the ncRNA family

ncRNA are divided into two types one is ncRNAs with household and another one is ncRNA with the regulatory, this is classified with the size and roles of it. ncRNAs are highly involved in cellular function. This regulatory ncRNA is divided into 3 forms such

as p-element-induced wimpy-interacting RNAs (piRNAs), Regulatory ncRNAs include small-scale interference (siRNAs), and miRNA [54-56]. This ncRNA involved in the regulation is divided based on the nucleotide size such as less than 200 nt or more than 200 ntncRNAs piRNAs, These two ncRNAs such as miRNAs and piRNAs act as RNAs. lncRNAs are RNAs that extended with their capability to contain nucleotides numbers.

3.1 LncRNAs and their Functions

LncRNAs are endogenous RNA molecules, which contain 200-100,000 nucleotides. Approximately 7,000–23,000 lncRNAshave been identified in vivo, which is significantly higher than the number of protein-coding genes that have been found. LncRNAs exhibit an mRNA-like structure with a poly (A) tail in certain cases. LncRNAs lack a significant ORF and protein-coding function and are involved in the regulation of gene expression at the epigenetic, transcriptional, and post-transcriptional levels in the form of RNA [57]. LncRNAs regulate gene expression and chromatin structure in the following ways: i) Decoy effect: Binding to other RNAs and proteins to alter their functions; ii) scaffold effect: Connecting chromatin modified proteins and DNA regions to form signal connections; iii) post-transcriptional effect: Forming RNA dimers with mRNA sequences to block transcription-associated sites, subsequently regulating the stability, cleavage, and translation of protein-coding genes [58].

3.1.1. LncRNA Roles in Cancer

A large number of lncRNAs can promote tumor growth and metastasis. PVT1 is required for a high level of c-Myc protein; PVT1 RNA and c-Myc protein expression is highly correlated in primary human tumors. Suppression of PVT1 inhibits c-Myc-driven tumorigenic potency [59]. MALAT1 was first identified in lung cancer MALAT160 and is

one of the most studied lncRNAs in cancer. For example, MALAT1 can promote tumorigenesis through the Wnt/β-catenin pathway, epithelial-mesenchymal transition, PI3K/AKT pathway, ERK/MAPK pathway, and angiogenesis [61]. PCAT-1 functions as a prostate-specific regulator of cell proliferation and it has been implicated in a subset of prostate cancer patients [62]. PCGEM1 is a prostate cancer-specific lncRNA; it can promote cell proliferation and reduce apoptosis induced by anticancer drugs [63,64] HOTAIR is up regulated in breast tumors and its expression is strongly associated with breast cancer metastasis and patient survival [65]. Finally, LINK-A expression and activation of LINK-A-dependent signaling pathway correlate with triple-negative breast cancer, and they together promote breast cancer glycolysis reprogramming and tumorigenesis [66]. Moreover, LINK-A-dependent AKT hyperactivation can lead to tumorigenesis and resistance to AKT inhibitors [67].

Much of the evidence for this comes from genome-wide studies that reveal that transcription factors, such as p53 [9,68,] MYC or the estrogen receptor [69], or signaling cascades such as Notch, specifically regulate the expression of a substantial number of lncRNAs[70]. For example, after DNA damage or oncogenic stress, the transcription factor p53, a preserver of cellular homeostasis, initiates a tumor suppressor program that involves the induction of many genes, including dozens of lncRNAs. Some of these are direct transcriptional targets of p53. Among them, the mouse tumor protein p53 pathway corepressor 1 lincRNA-p21 (Trp53cor1) promotes apoptosis by contributing to p53-dependent transcriptional repression through its interaction with the protein heterogeneous nuclear ribonucleoprotein K (Hnrnpk) [9]. In addition, the human lncRNAs (PANDAR) [71] and LINC-PINT [72] act as regulators of p53-dependent apoptosis and cell cycle arrest,

depending on the cellular context, by mediating transcriptional and epigenetic repression of gene expression, respectively. In contrast, the lncRNA induced by p53 lncRNA activator of enhancer domains (LED), contributes to p53 transcriptional regulation by interacting with p53 transcriptional enhancers[73]. Consistent with their role in the p53 response, several human p53-regulated lncRNAs are downregulated in colorectal cancer[72], similarly to LED, epigenetically silenced in acute lymphocytic leukemia, among other tumor types [73], suggesting a role for them as tumor suppressors. In addition, other lncRNAs are involved in the p53 network without necessarily being transcriptional targets of p53, such as the maternally expressed gene 3 (MEG3) lncRNA, which is downregulated in multiple cancers, is involved in p53 regulation and has a concomitant effect on cell survival and proliferation [74].

4. Changing Effects of Polyphenols in Cancer with Main ncRNAs

4.1. miRNAs Tracking by Polyphenols

Different studies are showing that plant-based polyphenols are having anti-cancer properties in all types of cancers [75-77]. This review shows inclusive of enhancement of different ways which are involved in apoptosis in cancer cells [78-81]. Apart from these changes, there are 3 types of epigenetic changes such as modification of chromatin structure, methylation of DNA, and miRNA effect are determined in the polyphenol treated cancerous cells [82]. In specific, these three polyphenols such as curcumin, EGCG, and resveratrol deregulate different groups of miRNAs, which are found in all stages of cancer development, which further shows anti-cancer potential. From this, we could conclude that the deregulation of the enhancement of miRNA involved in different cancer by suppressing the tumor genes, thus it shows the anti-tumor potential of polyphenols (Figure 2) [83-85].

4.1.1. Tracking of Polyphenol Oncogenes of miRNAs

A specific miRNA that belongs to the oncogenic group is miR-17. The augmentation of this miR-17 causes enhanced growth, migration of cells with metastasis, and decreased apoptosis [86-88]. The other polyphenol, resveratrol has action in prostate cancer by decreasing the level of phosphatase and tensin homolog (PTEN). The increased expression of the miR-17 oncogene band shows the decreased expression of the other miRNA-s such as mir-20a, miR-106a, and mir-106b in the prostate cancerous cells (DU145) upon treated with resveratrol (50 μM)89,90. Along with that, the enhanced expression of these miRNAs by resveratrol leads to decreased expression of the PETN protein and mRNA [91].

The sheltered PTEN protein and mRNA levels by pterostilbene develop an abridged tumor in vivo in solid tumors such as prostate and hematological, systemically found in the circulation, with the decreased expression of miR-106a-5p and miR-17-5P [89]. EGCG has protected effects on the NSCLC cells treated with the cisplatin, which further impairs the expression of the has-miR-98-5p by enhancing the expression of p53 [92]. The mango polyphenols modulate the oncogenic miRNA-21 that breast cancer with metastatic (MDA-MB231) cells. The miRNA-7 is targeted by genistein in the ovarian cancer cell [93]. Similar to this, the other miRNA which is targeted by the quercetin and hyperoside (0–60 μg/mL) are miRNA-27a for modulating the renal cancer cells resistance properties [94].

4.1.2. miRNAs Tracking as Polyphenol Tumor SuppressorGenes

The polyphenol, curcumins enhance the antitumor effects found in diverse cancer cells and have an effect with miRNAs and protein target [95,96]. Interleukin obligatory factor 2 (ILF2) could act as an oncogene and be found to be linked with the metastasis and

pancreatic carcinoma (PANC-1) cell invasion [97]. Upregulation of miR-7 by curcumin, which acts as a suppresser of oncogene which impairs the expression of ILF2 in PANC-1, further it causes cell apoptosis [98]. Along with that curcumin with different dosages could enhance the expression of miR-378 mediates the expression of targeted p38 expression. This results in the commencement of the p38 signaling pathway, which further impairs the proliferation of the glioblastoma and (U87) cell apoptosis [99]. 15 μM of curcumin in A549 cells could regulate the expression of the p53 and miR-192-5p/215, by forming an innovative target of transcription for miR-192-5p/215, the X-linked Apoptosis Inhibitor (XIAP) (p53 wild-type) 100. In the arrangement, the anti-oncogenic mechanism of curcumin was connected with induction of miR-340-XIAP, and activation of p53-miR-192-5p/215-XIAP in non-small-cell lung cancer [100,101]. 25mM of curcumin impairs the expression of chemical ligands (CXCL2 and CXCL1) in MDA-MB-231 cells by miR-181b up-regulation and, which further causes apoptosis and development of cells [95,100,102].

Inflammation is an important factor for the growth of cancer and cell progression at a metastatic level. Curcumin impairs the level of the pro-inflammatory cytokine such as CXCL1 and 2 which further leads to attenuated breast cancer metastasis development. This shows that it could suppress the elution of the CXCL1 and 2proinflammatory cytokines, leading to decreased development of breast cancer metastases. This suggests that the antitumor effect of curcumins is connected to the activity of inflammation [103]. Treatment of curcumin (10μM) in DU145 cells restores the progression of miR-143 and activates the phosphoglycerate kinase 1 expression (PGK1) to pin down the proliferation and migration of cell [104].Curcumin in prostate cancer activates the most vital transducer such as forkhead D3 (FOXD3) was also an important transducer. This synergizes with the curcumin and

impairs the tumor cell progression [104].miR-143 has a different role such as vascular homeostasis and muscle cell maintenance, etc., this leads to determine the new application with curcumin [105,106].

4.2. Tracking of Polyphenol with lncRNAs

LncRNAs are found to be active during the regulation of tumor progression. Plant polyphenols are determined to have an anti-cancer effect via lncRNA oncogenic suppressor gene promotion or impairing lncRNAoncogenes which results in a growing focus on lncRNAs in cancer research. The different mechanisms of antitumor with the lncRNAs regulation by the polyphenols are shown in Figure 3.

4.2.1. Tracking of Polyphenol Oncogenes of lncRNAs

Treatment with curcumin prevents human prostate cancer stem cells (HuPCaSCs) via invading, proliferating, and decreasing tumor origins [107]. treatment with curcumin protects from the production of lncRNA-ROR and attenuated miR-145 to mediate the development of cells, metastasis, and invasion [108]. LncRNA-H19 is found to be initially confirmed oncogene in breast tumors of humans [109,110]. There is a high expression of H19 found in gastric cancer cells [111,112]. Along with that, there is an encouragement of H19 development by c-Myc, which in detent apoptosis by p53 in cancer cells. Treatment of 50 μM of curcumin inhibits the level of c-Myc and H19 levels found in gastric cancer cells 113. The other lncRNA inhibited by the curcumin is Translocalization 1 (PVT1) [114].

There is a decreased proliferation, metastases, and invasion in PC cells by the disconnecting PVT1, which are found to be sensitive to gemcitabine [115,116]. There is a modulation of lncRNA by EGCG and resveratrol [117]. There is a down-regulation of

LncRNAAK001796, oncogene could prevent progressing of NSCLC cells [118]. Wnt-β-catenin is highly found to be involved in one pathway. The wnt/β-catenin pathway would be supported by MALAT1 which is involved in the attenuation of tumor cell metastasis and invasion [119]. There is an inhibition of nuclear β-catenin via impairing MALAT1 by resveratrol [119]. There is an inhibition of HOTAIR with PC's expression by Genistein which is an oncogenic lncRNA found in different types of cancers [120]. In breast cancer, the phytochemical compound has an anti-tumor function which is a similar function as PC in HOTAIR 121.

4.2.2. Tracking lncRNA Tumor SuppressorGenes by Polyphenols

Curcumin augments the expression of MEG3 in ovarian cancer (OC). The increased expression of MEG3 inhibits miR-214 [122]. A low level of curcumin (1 μM) attenuates the resistance to a chemical in ovarian cancer through the MEG3-miR-214 axis [122]. Along with that, there is a modification of nuclear-induced autosomal transcript 1 (NEAT1) by EGCG. It incites the inhibitory effect of cells with cisplatin via inhibition of miR-98-5p in lung cells which induces chemical resistance by CTRI [123]. The cancer stem cells (CSCs) can mediate resistance to chemotherapy, tumor recurrence, and tumor metastasis [124]. NEAT1 knockdown in NSCLC cells attenuates the level of CSC features. This NEAT1 gene expression may make a payment to stemness [123,125]. There is an attenuated stemness by reduced EGCG level via induction of CTR1 with over-expressing NEAT1 [123]. The polyphenols which have an anti-cancer effect found to resolve the oncogenes of main ncRNA. This mediates ncRNAs to mitigate the suppressant function of tumor[125-127].

Conversely, there is no mechanistic research has been elucidated although there are different ncRNAs classes with length, Its features have found to be recognized in the

literature. It shows that ncRNA classes/sub-classes could be mediated by the effect of anti-carcinoma. The anti-cancer effect of polyphenol on other ncRNAs needs to be properly established in the future. The growing data communally illustrates that ncRNAs with tumor-suppressing ncRNAs and carcinogenic. In meticulous, this polyphenol treatment tenders innovative solutions for the treatment of cancer.

5. Challenges and Viewpoints

There exists emerging innovative, positive approach for utilization of plant polyphenols for different types of cancers. With respect to this, there is a proper investigation required on the topics as detailed below:

(a). There are many attempts to augment the bioavailability and attenuate the limited potential through modification of chemical and development synthetically; nano-structures. This further helps to multiply pathologies of cancer in a better manner.

(b) The polyphenol anti-tumor properties with their analogs and ncRNAs with other forms need to be focused on.

(c) The safety and efficacy of polyphenols in clinical trials need to be established. Dysregulation of ncRNA needs to be concerned in other diseases apart from cancer.

Therefore, sepsis clinical trials are required to be a timely but merely ephemeral concern. These are predictable to be extremely enlightening concerning the ncRNAs therapeutic efficacy.

6. Conclusion

ncRNAs acts as a central regulator for cancer via different mechanisms. Polyphenols present in the plant promotes the tumor suppressor of ncRNA or impair ncRNA oncogenes action in various form of cancers. There is an investigation of polyphenol is needed with the miRNA level or LncRNA or the passageway level or the gene. In this review, we have captured the mechanistic roles of the polyphenol and the major ncRNAs as well. This suggests that polyphenols present in the plant could act as an antitumor agent. This safeguards the normal cells and serves patients to kill cancer cells.

Conflict of Interest

The authors declare no conflict of interest.

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Figure Legends

Figure 1. The meticulous classifications and sources of plant-based polyphenols.

Figure 2. Antitumor mechanisms of representative polyphenols implicated in regulating miRNAs.

Figure 3. Anti-tumor mechanisms of representative polyphenols involved in regulating lncRNAs.

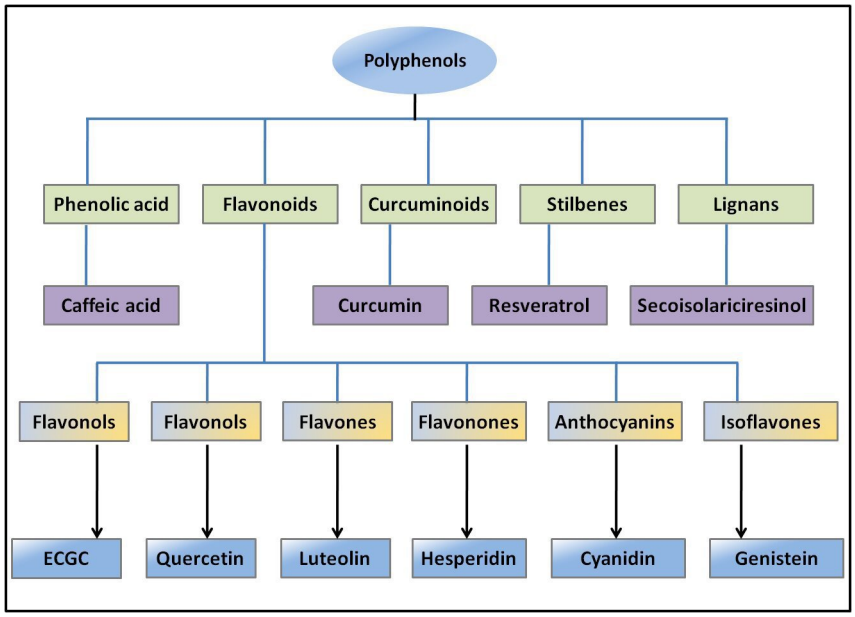

Figure 1 final.jpg

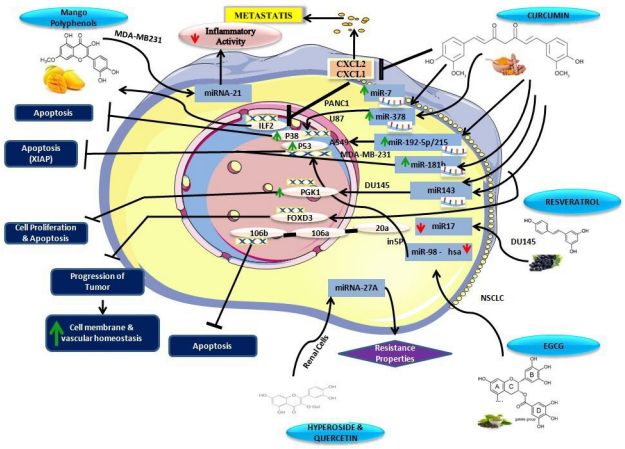

Figure 2 final.jpg

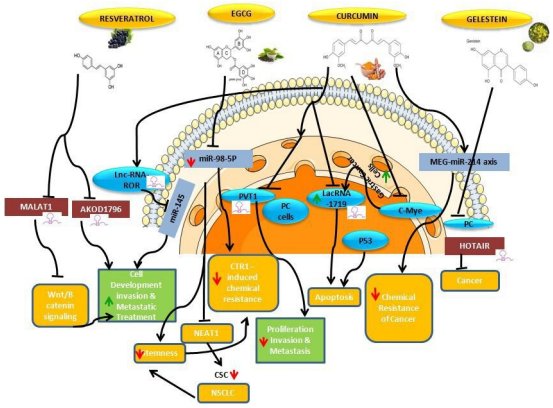

Figure 3 final_1.jpg

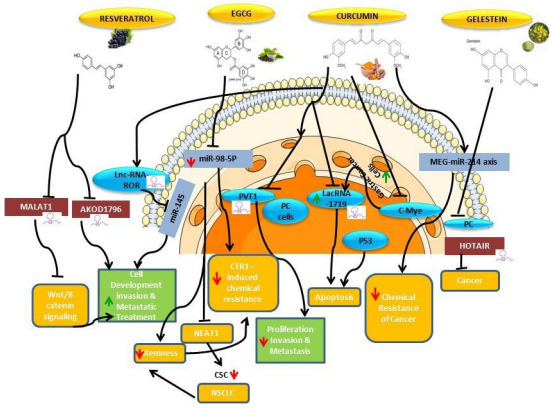

Figure 3 final_2.jpg