



Abstract

The Use of Natural Products of Epigenetic Modulators in Anti-Cancer Drug Studies [†]

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Abstract: The natural products obtained from plants, bacteria, fungi and marine have been used in the treatment of human diseases throughout the centuries. These compounds of them also interfere with the expression of genes by influencing epigenetic mechanisms. Recent researches showed significant outcomes suggesting that epigenetic silencing of the main regulatory genes is a sign of cancer onset and its progression. Epigenetic mechanisms that regulate expression of genes without mutation in the DNA are carried through DNA methylation, histone modification, chromatin remodeling and RNA interference. DNA methylation observed in the promoter regions of genes and prevents binding of the transcription factors by suppressing gene expression or by altering the nucleosome package of DNA, and may also directly inhibit transcription. Plant based products, such as curcumin, flavonoids, genistein, have been shown to exhibit cytostatic and apoptotic activities by influencing DNA methylation-based gene expression regulation in tumor cells. Additionally, natural products such as sulforaphane, retinoic acid, cucurbitacin B, casein Q, parthenolide, folate, cobalamin, pyridoxine and methionine also are used as anti-cancer agents based on DNA methylation. On the other hand, microRNAs (miRNAs) play a particular role in the epigenetic regulation of gene expression in post-transcription and post-translation processes. Quercetin, tryptolide, and honokiol are the natural compounds used in miRNA based agents. Histone modifications, which also affect the chromatin structure, play an important role in the initiation and progression of carcinogenesis as well as regulation of gene expression. As expected particular inhibitors of histone acetyltransferases (HATs) and histone deacetylase (HDAC) enzymes which are responsible of histone modifications have been developed for epigenetic intervention in cancer treatment. Numerous natural compounds are known to affect histone-modifying enzymes; such as romidepsin, epigallocatechingallate (EGCG), daidzein, sulforaphane, glucoraphanin, parthenolide, triptolide, sinapinic acid. Natural epigenetic modulators developed for epigenetic mechanisms enable the destruction of apoptotic, necrotic or autophagic pathways of tumor cells. Beside epigenetic mechanisms, these products exert their effects through influencing the cell cycle, DNA repair, and epigenetic mechanisms which modulate gene expression. More extensive in vitro and in vivo studies are required to investigate the effect of natural product-based epigenetic agents which seems to be very promising for future cancer treatment approaches.

Keywords: epigenetics; natural products; cancer therapy; anti-cancer drug studies



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