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Short Communication

Targeting Telomerase and Topoisomerase-II by Natural Moieties: An Anti-Cancer Approach

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One of the fundamental characteristic of tumor cell is to maintain the telomere length for continues progressive growth and survival. For the same, tumor cell has elevated levels of telomerase enzyme[1]. Telomerase is an unusual enzyme that acts on parts of chromosomes known as telomeres. Telomerase is a ribonucleoprotein and expressed in approximately 85% of different human cancers[2]. There is strong evidence for the existence of an important relationship between telomeres, telomerase and cancer [3]. Normal human cells progressively lose telomeres with each cell division until a few short telomeres become uncapped leading to a growth arrest, known as replicative aging. This phenomenon is totally absent in the cancer and cancer cells are adapted to have higher levels of telomerase enzyme which results in uncontrolled cell division. Attempts have also been made to develop telomere length-and telomerase-based diagnostic tools and anticancer therapeutics [4]. Secondly, topoisomerase-II (Topo-II) also attracts researchers that could be another target for anti-cancer therapy. Topo-II itself required for DNA replication, transcription and chromosome segregation. Because Topo-II is crucial for genomic integrity, interference in its activity might be an effective strategy for cancer chemotherapy. Although there are etoposide and doxorubicin anti-cancer drugs for Topo-II but development of therapy resistance restricts their ability. The phytochemicals including flavonoids and xanthonoid are known to possess strong cancer inhibitory action due to their action against telomerase and Topo-II. There is plenty ofwork available which is supporting the fact. For instance, Tawani and Kumar, found the role of quercetin against human telomerase enzyme[5].Study on MGC-803 and SGC-7901 human gastric carcinoma cells explored that Gambogic acid (GA) suppresses telomerase activity and telomerase reverse transcriptase (TERT) mRNA level via down-regulation of c-Myc oncogene expression[6]. Further, Wu et al. [7] reported GA mediated inhibition of human lung carcinoma growth using of SPC-A1 cell and xenograft nude mice model due to negatively regulation of telomerase/hTERT expression.Similarly, couple of *in-vivo* and *in-vitro* studies has been carried out on human hepatoma SMMC-7721 cells and demonstrated dose and time dependent inhibitory effect of GA on telomerase activity[8,9].Moreover, GA was also found to modulate the post-translational modifications of hTERT via Aktsignalling dependent mechanisms[10]. Genistein (GEN) induces growth arrest in association with telomerase inhibition in brain tumor cells via the suppression of TR- and TERT mRNA[11]. In addition,Cantero et al. [12] performed a comparative study in Chinese hamster ovary AA8 cells and showed that the flavonoids, luteolin and quercetin are topo II inhibitors.GEN inhibition of Topo-II expression through the regulation of Specificity protein 1 and Specificity protein 3 and HeLa cell apoptosis[13].Hence after looking at the data author(s) would like to divert researcher toward flavonoid's anti-cancer activity mediated through telomerase and Topo-II inhibition.

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