and signalling pathways, regulated by pharmacologically active compounds, presents novel opportunities for the targeted treatment of cancer. The aim of this review is to highlight the potential role of these compounds for context-specific anticancer therapy.

Key words: autophagy; natural and synthetic compounds; signalling pathways

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Phytomedicines: Resolution for inflammatory disorders

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Abstract: Phytomedicines have been used for treating or preventing diseases throughout human history. We have been conducting in exploration of traditional or folk herbal medicines as an attempt to identify novel phytocompounds candidates for further development into botanical supplements or drugs for inflammation related diseases, including cancer, acute liver hepatitis, and sepsis. Comparative "OMICS" technology platforms in combination with various *in vitro* and *in vivo* cell- and gene-based bioassays, murine skin inflammatory and syngeneic and xenograft mammary tumor and melanoma models are employed to validate the pharmacological effects and the underlying mechanistic insights of the identified bioactive phytocompounds. The therapeutic potential of phytoagents, alone or in combination, in sensitizing the chemotherapeutic drug efficacy and/or reduction of its side effects in tumor-bearing mice are investigated. In addition, how phytoagents modulate pro- or anti-inflammatory lipid mediators, such as oxylipins, and related signaling cascades systemically or at organ levels are also addressed for understanding sepsis or cancer pathogenesis and the modes of action of bioactive phytoagents.

Key words: plant galactolipids; inflammatory disorders

Potential application of gamma-tocotrienol as a novel chemosensitizer in gastric cancer

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Abstract: Gamma-tocotrienol, a member of vitamin E superfamily has attracted great attention of late for its anti-proliferative and anti-carcinogenic potential against different cancers. For example, our group had previously reported that anti-proliferative and chemosensitizing effects of γ-tocotrienol are associated with its ability to suppress activation of signal transducers and activator of transcription 3 (STAT3), a pro-inflammatory transcription factor that plays a pivotal role in the survival, proliferation, angiogenesis and chemoresistance of hepatocellular carcinoma. However, the potential of gamma-tocotrienol to overcome chemoresistance in gastric cancer, which is one of the deadliest cancers in Asia-pacific region, has never been explored before. Hence, we analyzed the efficacy of gamma-tocotrienol in combination with capecitabine to modulate tumor growth and survival in gastric cancer cell lines and xenograft mouse model. Cell proliferation and apoptosis assays indicated that gamma-tocotrienol potentiated capecitabine induced programmed cell death in various gastric cancer cell lines. Gamma-tocotrienol also inhibited expression of Bcl-2, Bcl-xL, cyclin-D1, COX-2, ICAM-1, VEGF, CXCR4, MMP-9 proteins, induced PARP cleavage and inhibited constitutive and capecitabine-induced NF-κB activation in gastric cancer cells. *In vivo* studies using xenograft model of human gastric cancer demonstrated that gamma-tocotrienol alone suppressed tumor growth and this effect was further potentiated in conjunction with capecitabine. Also the markers of proliferation index Ki-67 and the micro vessel density CD31 were signif-

icantly downregulated in tumor tissues by the combination of capecitabine and gamma-tocotrienol. As compared to the vehicle control, gamma-tocotrienol further suppressed the NF-κB activation and expression of cyclin D1, COX-2, ICAM-1, MMP-9 and survivin in tumor tissues obtained from treatment groups. Overall our results suggest for the first time that gamma-tocotrienol can potentiate the effects of capecitabine through modulation of multiple markers of proliferation, invasion, angiogenesis and metastasis in gastric cancer.

Key words: gastric cancer; gamma-tocotrienol; chemosensitizer

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Epigenetic alterations and cancer chemoprevention by dietary polyphenols

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Abstract: Growing evidence indicates that cancer incidence across the world is not similar, and it is more prevalent in certain populations than others, suggesting the critical role for dietary and lifestyle factors. For instance cancer incidence among people from the Indian subcontinent, where most spices are consumed, is much lower than that in the Western World. Spices have been consumed for centuries for a variety of purposes e.g. as flavoring agents, colorants, and preservatives. However, there is increasing evidence for the importance of plant-based foods in regular diet to lowering the risk of most chronic diseases, so spices are now emerging as more than just flavor aids, but as agents that can not only prevent but may even treat disease. Besides suppressing inflammatory pathways, spice-derived nutraceuticals can suppress survival, proliferation, invasion, and angiogenesis of tumor cells. Increasing evidence indicates that genetic alterations are relatively rare, and epigenetic changes (DNA methylation, histone modifications and expression of noncoding RNAs) plays a bigger role in human cancer, and can be easily influenced by environmental, lifestyle and dietary factors, and some estimates suggest that over two-thirds of the cancer incidence can be accounted for by the environmental and dietary factors alone. Among all these factors, diet is probably the single most important factor which may influence carcinogenesis more comprehensively, because diet is readily modifiable and have the potential to modulate multiple epigenetic processes. Polyphenols in dietary botanicals represent a versatile group of phytochemicals with many potentially beneficial activities in terms of disease prevention. Dietary polyphenols (bioflavanoids) have antioxidant and anti-inflammatory properties that might explain their chemopreventive effects. However, the actual therapeutic potential of these compounds may not have been completely realized due to lack of understanding on the effects of these agents on epigenetic modifications. Recent, but limited evidence indicates that some of the polyphenols, including curcumin (from turmeric), genestein (from soy), EGCG (from green tea), diallyl disulfide (from garlic), sulforaphane (from broccoli) and resveratrol (from grapes) may induce epigenetic changes in various cancer cell lines. This presentation will describe some of the current scientific evidence for the role of epigenetic alterations induced by curcumin and boswellia, in support of their anti-cancer activities, which provides a strong scientific foundation for preclinical and human clinical intervention studies in future.

Key words: polyphenols; cancer ;chemoprevention; dietary; epigenetics

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