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This study assessed the use of astaxanthin as an anticancer agent for increasing inhibition to melanoma cells (A375 and A2058). Wound healing and invasion assays presented that astaxanthin treatment reduced melanoma cell migration in a dose-dependent manner. The effects on melanoma cell migration were conferred via suppressed expressions of matrix metalloproteinases 1, 2 and 9. Dichlorofluorescein diacetate assay further showed that astaxanthin treatment reduced production of cellular reactive oxygen species. Cellular proliferation assay revealed potent dose-dependent inhibiting effects on melanoma cells. One-dimensional flow cytometric analysis demonstrated that astaxanthin induced cell cycle arrest in G1 phase. Mechanisms of apoptosis were verified by double fluorescence staining with annexin V-fluorescein isothiocyanate and propidium iodide. The antitumor effects of astaxanthin significantly decreased tumor size in a xenograft model. In summary, the experimental results showed that astaxanthin has potent *in vivo* and *in vitro* inhibiting effects on melanoma tumor growth for developing as chemotherapeutic agents.

Equisetum ramosissimum, a genus of Equisetaceae, is a medicinal plant that can be separated into ethyl acetate (EA), dichloromethane (DM), n-hexane (Hex),methanol (MeOH), andwater extracts. EAextract was known to have potent antioxidative properties, reducing power, DPPH scavenging activity, and metal ion chelating activity. This study compared these five extracts in terms of their inhibiting effects on three human malignant melanomas: A375, A375.S2, and A2058. MTT assay presented the notion that both EA and DMextracts inhibited melanoma growth but did not affect the viabilities of normal dermal keratinocytes (HaCaT) or fibroblasts. Western blot analyses showed that both EA and DM extracts induced overexpression of caspase proteins in all three melanomas. To determine their roles in melanogenesis, this study analyzed their *in vitro* suppressive effects on mushroomtyrosinase.All extracts except for water revealedmoderate suppressive effects. None of the extracts affected B16-F10 cells proliferation. EA extract inhibited cellular melanin production whereas DMextract unexpectedly enhanced cellular pigmentation in B16-F10 cells. Data for modulations of microphthalmia-associated transcription factor, tyrosinase, tyrosinase-related protein 1 and tyrosinase-related protein 2 showed that EA extract inhibited protein expression mentioned above whereas DMextract had the opposite effect. Overall, the experiments indicated that the biofunctional activities of EA extract contained in food and cosmetics protect against oxidation, melanoma, and melanin production.

Melanoma is the deadliest cancer. We identified 7-hydroxydehydronuciferine (7-HDNF) isolated from the leaves of Nelumbo nucifera Gaertn cv. Rosa-plena to be a bio-active agent that antagonizes melanoma tumor growth in mice xenograft model *in vivo*. Cell proliferation assay demonstrated strong anticancer effects of 7-HDNF to exhibit a dose-dependent behaviour and displayed minor cytotoxicities on normal human skin cells, including epidermal keratinocytes and melanocytes, and dermal fibroblasts. With acridine orange (AO) staining and flow analysis, we found 7-HDNF induced the formation of intracellular vacuoles and the augmentation of acidic vesicular organelles (AVO). The apoptotic cell death ratio was measured via two-dimensional flow cytometry by annexin V-fluorescein isothiocyanate (FITC)/propidium iodide (PI) double stained to confirm the cellular membrane asymmetry lost. Onedimensional flow cytometric analysis showed 7-HDNF increased the cellular arrest in cell cycle at the G2/M phase. Through Western blot examinations, protein expressions were discovered to verify autophagy and apoptosis response mechanisms sharing the associated pathways. Finally, 7-HDNF presented a high-quality antimigratory activity in wound-healing assay. Overall, 7-HDNF presented high-quality anticancer bio-functions and inhibited melanoma tumor growth *in vivo* and *in vitro*.

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Bromodomain-containing protein 4 (BRD4) has recently emerged as an attractive epigenetic target for anticancer therapy. In this study, an iridium(III) complex is reported as the first metal-based, irreversible inhibitor of BRD4. Complex 1a is able to antagonize the BRD4-acetylated histone protein– protein interaction (PPI) *in vitro*, and to bind BRD4 and down-regulate c-myc oncogenic expression in cellulo. Chromatin immunoprecipitation (ChIP) analysis revealed that 1a could modulate the

interaction between BRD4 and chromatin in melanoma cells, particular at the MYC promoter. Finally, the complex showed potent activity against melanoma xenografts in an *in vivo* mouse model. To our knowledge, this is the first report of a Group 9 metal complex inhibiting the PPI of a member of the bromodomain and extraterminal domain (BET) family. We envision that complex 1a may serve as a useful scaffold for the development of more potent epigenetic agents against cancers such as melanoma.

Three new butanolides, isophilippinolide A, philippinolide A, and philippinolide B, and an amide, cinnaretamine, were isolated from the roots of Cinnamomum philippinense to be identified by spectroscopic analysis. Four isolated compounds were screened to examine their radical-scavenging ability, metal-chelating power, and ferric-reducing antioxidant power assay (FRAP). Cinnaretamine showed powerful antioxidative properties in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay and a reducing activity; all compounds presented minor inhibition of metal-chelating capacities. The effects of anti-tyrosinase of C. philippinense constituents were determined by the level of the suppression of hydroxylation that turned from L-tyrosine to L-dopa through an *in vitro* mushroom tyrosinase assay, and all testing samples illustrated slight mushroom tyrosinase inhibitory properties. Isophilippinolide A exhibited inhibitory effectivenesses against the A375.S2 melanoma cell line in a cell viability assay at concentrations ranging from 0 to 200 μM for 24 h. Propidium iodide staining and flow cytometry analyses were applied to assess cell cycle accumulative distribution. It was discovered that isophilippinolide A caused sub-G1 phase accumulation in positive correlation for apoptosis to inhibit cell growth. Further investigation revealed that isophilippinolide A induced A375.S2 cells with an increase of caspase-dependent apoptotic proteins to trigger correlated pathway mechanisms according to Western blotting results. Finally, isophilippinolide A displayed only low cytotoxicities to human normal epidermal cells (melanocytes) and dermal cells (fibroblasts). Altogether, the results implied C. philippinense compounds could be considered functional ingredients in cosmetics, foods, and pharmaceutical products, particularly for their anticancer ability on human skin melanoma cells. Kinetically inert metal complexes have arisen as promising alternatives to existing platinum and ruthenium chemotherapeutics. Reported herein, to our knowledge, is the first example of a substitutionally inert, Group 9 organometallic compound as a direct inhibitor of signal transducer and activator of transcription 3 (STAT3) dimerization. From a series of cyclometalated rhodium(III) and iridium(III) complexes, a rhodium(III) complex emerged as a potent inhibitor of STAT3 that targeted the SH2 domain and inhibited STAT3 phosphorylation and dimerization. Significantly, the complex exhibited potent anti-tumor activities in an *in vivo* mouse xenograft model of melanoma. This study demonstrates that rhodium complexes may be developed as effective STAT3 inhibitors with potent anti-tumor activity.

Biography

Hui-Min David Wang, a Full Professor at Graduate Institute of Biomedical Engineering (National Chung Hsing University), graduated from the Department of Chemical Engineering, National Cheng Kung University, Tainan, Taiwan. In 2014, he got Ta-You Wu Memorial Award which is the highest price to young scientist of Ministry of Science and Technology (MOST) in TW. In 2015, he got Young Scholars Biotechnology Invention Award which is the highest price to young scientist of Taiwan Society of Biochemistry and Molecular Biology (TSBMB) in TW. In 2016, he got the Precious Stone Award in TW.

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