



Prospective Role of Maslinic Acid in Anticancer Therapy and Cytoprotection

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Dear Editor

Cancer is still an insurmountable problem that has a devastating impact on public health all over the world. According to estimates, there will be 26 million new cases of cancer and 17 million annual cancer deaths by the year 2030 [1]. Extreme oxidative stress, persistent inflammation, cell cycle abnormalities, aberrant proto-oncogene expression, angiogenesis disorders and other factors all contribute to the complicated and multi-faceted manifestation of cancer [2]. In the midst of various type of cancer, the top most prevalent carcinomas are breast, lung, colon and prostate cancers. According to World Health Organization (WHO), in terms of new cancer cases, breast cancer accounted for 2.26 million cases, lung cancer accounted for 2.21 million cases, and colon cancer accounted for 1.93 million cases. The most commonly mutated tumor suppressor genes involved

in cancers are BRCA1, BRCA2, and p53 and mutated oncogene HER2 and RAS family genes [3]. Chemotherapy, radiation and surgical resection are frequently used as cancer treatments. Surgical removal in early stage of solid tumor is fruitful. Combination therapy uses a variety of therapies, including surgery, chemotherapy, and radiotherapy. The conventional therapies are consequence to significant side effects with high morbidity rates, and frequent relapse developed drug resistance [4]. So, evolution efficient, novel and selective bioactive formulations against cancer treatments are immediately warranted. Recently, triterpenes have gained tremendous attention in nanobiotechnological research due to their biocompatibility, availability, renewable nature, and regulated degradability. Maslinic acid [MA, (2 α ,3 β)- 2,3-dihydroxylolean-12-en-28-oic acid] is one of



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the oleanane type triterpene, exerted extensive range of medicinal activity like anticancer, anti-inflammatory, antidiabetic, cardio protective, hepatoprotective and many more [5]. 3D-QSAR modelling of MA was performed and ADMET, molecular docking evaluated its anticancer target, pharmacophore design and drug discovery potential against breast cancer [6]. Cytotoxic nature of MA was extensively studied against various cancer cells and the experimental outcome revealed that MA altered cancer related protein expression in cellular level. Rufino-Palomares *et al.*, demonstrated that MA efficiently modulated apoptosis via caspase 3 activation, elevating Bax expression whereas Bcl2 level significantly diminished. All these events eventually activated Jak-STAT signalling pathway [7]. MA also, in a time- and dose-dependent manner activated the extrinsic apoptotic pathway, which was observed in Caco-2 colon cancer cells. In this study, Caspase-8, caspase-3 cascade were activated with enhance expression of Bid protein [8]. Anti-metastasis and anticancer activity of MA was elucidated on *in vivo* and *in vitro* experiment by monitoring AMP-mTOR pathway [9]. MA played anti-angiogenic role in endothelial cell by inhibiting the chief moderator VEGF and hindered renal cancer cell proliferation [10]. The anti-tumorigenic, anti-apoptotic and Anti-metastasis potential of MA on pancreatic cell was achieved through observing proliferation, migration and also transcriptomics and proteomics [11]. MA exerted inhibition in cell proliferation and migration in brain tumor cell through MAPK cascade signaling pathway [12]. It also regulated cell cycle and proliferation of colorectal cancer cell in time and dose dependent manner through inhibiting cell cycle regulatory protein like Chk1 and CyclinD1 as well as inflammatory pathway also activated through NF- κ B and IKK- β signaling pathway [13]. In an *in vivo* study with BALB/c leukemic mice model, MA efficiently moderated immune response by increasing macrophage and NK cell activity. Here, CD19 and CD11 population markers were also increased which might be responsible for the cytotoxicity effects NK cells and enhancement of phagocytic activity of macrophages[14]. The conventional therapies likewise chemotherapeutic drugs, monoclonal antibodies targeted tyrosine kinase receptor and other anti-metastasis drugs shown undesired toxicity towards healthy physiological system mainly cardio-vascular system and also increase the risk of thrombotic proceedings. Macrophages play a crucial role in cancer development through modulating inflammatory pathways. In case of solid tumor, the M1/M2 ratio of macrophage augmented cancer survival. MA prevented chronic inflammation via modulating IL-8, IL-1 α , and IL-1 β expression [15]. In another experimental study, MA elevated HO-1 expression rather than COX-2 and iNOS in LPS induced HUVEC cell [16]. MA exerted protective activity in HUVECs through NF- κ B inhibition either Nrf2 dependent or independent manner [17]. In endothelial cell MA inhibited apoptosis. The result showed mitochondrial dependent NLRP3 inflammasome expression that was reduced by SIRT1/Nrf2 pathway [18]. Triterpenoids gained a lot of interest for their self-assemble capability in various solvent without any external force. MA also formed self-assembly structure in common organic solvent [19]. We found that self-assemble MA (SA-MA) showed ameliorative role in DOX induced cytotoxicity against healthy blood cell [20]. The protective role of MA also was noted by reducing inflammation and other cellular stress through Nrf2 pathway. Self-assembly is a unique morphology of MA in which it exerts nano-vesicular structure that enters into the healthy cells and exhibits its protective activity against DOX induced oxidative stress. Further research on SA-MA in various cancer models will pave the way for its potential use as an organoprotective agent in chemotherapy

in addition to its potent anticancer activity.

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