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Effect of alcoholic extract of Ayurvedic herb *Tinospora cordifolia* on the proliferation and myeloid differentiation of bone marrow precursor cells in a tumor-bearing host

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Abstract

The present study investigates the effect of in vivo administration of alcoholic extract of *Tinospora cordifolia* whole plant (ALTC) on the proliferation and myeloid differentiation of bone marrow hematopoietic precursor cells in mice bearing a transplantable T cell lymphoma of spontaneous origin designated as Dalton's lymphoma (DL). BMC obtained from ALTC administered DL-bearing mice showed an enhanced BMC proliferation and colony forming ability in vitro in response to L929 conditioned medium as a source of colony stimulating factor (CSF). The number of granulocyte–macrophages colony (CFU-GM) was predominantly higher in the cultures of BMC obtained from ALTC administered mice as compared to mice injected with PBS alone. An increase in the count of bone marrow derived macrophages (BMDM) from ALTC administered mice was also observed along with an increase in the count of tumor associated macrophages. The BMDM obtained from ALTC administered mice showed an enhanced response to signal of LPS for activation to produce IL-1 and TNF. This study indicates that the *T. cordifolia* can influence the myeloid differentiation of bone marrow progenitor cells and the recruitment of macrophages in response to tumor growth in situ.
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Keywords: *Tinospora cordifolia*; Hemopoiesis; Dalton's lymphoma; Bone marrow derived macrophages

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1. Introduction

Tumor growth in general is invariably associated with the onset of immunosuppression in a tumor-bearing host [1–4]. Along with the tumor progression a concomitant inhibition or increase of hemopoiesis depending on the type of tumor has also been reported [5–8]. We have reported the effect of Dalton's lymphoma (DL), a transplantable T cell lymphoma of spontaneous origin, on the immune responses and hemopoiesis of the tumor-bearing host [9–15]. It was observed that progressive DL growth leads to suppression of hemopoiesis [5,15,16]. Moreover, a correlation was observed in the suppressed hemopoiesis and the immune status of the DL-bearing mice. Therefore, we were interested to develop a therapeutic protocol by which the DL-associated suppressed state of hemopoiesis could be reversed, in order to rescue the inhibited immune response of DL-bearing host.

A number of herbal agents have been reported to possess hemopoietic activity. *T. cordifolia*, an Indian medicinal plant used as a '*rasayana*' in Ayurvedic system of medicine, is currently being explored in our laboratory for its potential as therapeutic agent for the increase of host's antitumor immune responses. Extract of this herb has been demonstrated to augment the activity of murine peritoneal macrophages, T lymphocytes and B cells [17]. Moreover, *T. cordifolia* increases the leukocyte counts and reduces the neutropenia induced by single and multiple doses of cyclophosphamide [18]. We have reported that in vivo administration of extract of *T. cordifolia* induced a production of antitumor molecules like reactive nitrogen intermediates, tumor necrosis factor, IL-1 [19,20] and possesses a significant cytotoxicity [20]. Moreover, administration of *T. cordifolia* plant alcoholic extract (ALTC) also resulted in the activation of macrophages for various accessory functions such as antigen presenting ability and phagocytosis [20]. In view of the potent immunostimulations actions of *T. cordifolia* upon administration in vivo, we were interested to investigate if one of the causes of the increased immune response of tumor-bearing host could be traced back to an hematopoietic action of the herb. In the present study we report the effect of in vivo administration of ALTC on the myeloid differentiation of bone marrow cell (BMC) and on the functions of bone marrow-derived monophages (BMDM).

2. Experimental

2.1. Materials and methods

Tissue culture medium DMEM and most of the chemicals were purchased from Himedia (Mumbai, India). LPS and PHA were purchased from Sigma Chemicals Co. (St. Louis, MO, USA). All culture media were supplemented with 20 mg/ml gentamycin, 100 mg/ml streptomycin, 100 IU penicillin and 10% FCS (Himedia). All the reagents and ALTC used in the experiments were determined endotoxin free by the Limulus Amoebocyte Lysate Assay (sensitivity limit, 0.1 ng/ml).

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