**SUPPLEMENTARY DATA**

**Supplementary methods**

**Evaluation of the oral acute toxicity**

The evaluation of oral acute toxicity was carried out as per the Organization for Economical Cooperation and Development (OECD test 425) described procedure. Total 18 mice of either sex were divided into three groups (3 male & 3 female in each group) randomly *viz.* experimental groups 1 & 2 and control group 3 respectively. A day before an experiment, animals were kept on fasting. Next day, the ethyl acetate extract was administered orally using a 16G oral round ball tip feeding curved needles to the mice of the experimental groups. A single dose of 2000 mg/kg and 5000 mg/kg body weight were administrated among the mice of experimental group 1 and 2 respectively, while distilled water was administrated to the mice of control group. All mice were observed individually after first 30 min dosing, special attention was given during the first 4 h and followed up from 24 h to 14th day of the dosing to collect signs and symptoms of toxicity [54, 55]. The attention was paid to investigate the potential occurrence of tremors, convulsions, salivation, diarrhea, lethargy and drowsiness. Live weight of the animals was monitored on days 0, 7 and 14 of the dosing as one of the toxicity parameters. At the end of the experiment, the animals were sacrificed by cervical dislocation of anaesthetised animals and the organs *viz.* brain, stomach, liver, spleen, lungs, kidneys, muscles, esophagus and small intestine were collected to evaluate histopathological changes.

**Tumor model development**

EAC cell induced tumor model was chosen for this study, as it is of mouse origin and can be easily transplanted in immunocompetent mouse. The EAC cells were harvested from 75 cm2 cell culture flask with 70-80% cell confluence by trypsinization and followed by centrifugation at 750 rpm (Remi R8C) for 5 min. The harvested cells were diluted in 10 mM phosphate buffered saline (1X PBS) at a density of 5 × 106 cells, and 200 µl of viable cell solution were injected into the peritoneal cavity of each recipient mouse of 21±1 g body weight and allowed to multiply. The EAC cells were withdrawn from peritoneal cavity of the donor mice after 8–10 days of inoculation and diluted in 1X PBS and centrifuged at 750 rpm (Remi R8C) for 5 minutes and the cell pellet was resuspended in sterile 10 mM PBS which was injected (100 µl at 1 × 107 cells/ml) in left thigh of female mice for developing solid tumor [51, 56].

**Pilot study for effective dose determination**

After 4 days of EAC inoculation, a pilot study was set up for determination of effective dose in EAC induced tumor-bearing mice which were divided into four groups of 3 mice in each. The tumor-bearing mice were administered 200, 100 and 50 mg/kg body weight of ethyl extract of test drug in group 1, 2 and 3 respectively while100 µl distilled water was given to the mice of group 4 named as control once daily for 14 days [53] along with normal diet and water *ad libitum*. At the end of 14th days, the mice were sacrificed and tumors were dissected out for their volume calculation. Tumor size was measured by Vernier calipers using the formula V = 0.5 × a × b2, where ‘a' and ‘b' indicates the major and minor diameter, respectively.

**Supplement table 1**

Selective index of different extracts against cancer cell lines.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Selective Index** | **MCF-7** | **MDA-231** | **HCT-15** | **MIN6** | **EAC** | **L929** |
| **BLPE** | 14.92 | 5.07 | 4.69 | 24.61 | 3.79 | 1.00 |
| **BLEA** | **52.17** | 2.36 | 4.45 | 1.88 | 17.37 | 1.00 |
| **BLM** | 17.96 | 3.13 | 1.11 | 0.40 | 1.36 | 1.00 |

**Supplement table 2**

Observational study for BLEA oral toxicity in mice (OECD test 425).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Observation** | 0 h | | 0.5 h | | 1 h | | 2 h | | 4 h | | 24 h | | 14th day | |
| D1 | D2 | D1 | D2 | D1 | D2 | D1 | D2 | D1 | D2 | D1 | D2 | D1 | D2 |
| **Skin & fur** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Mucous membrane** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Tremors** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Convulsion** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Salivation** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Diarrhea** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Sleep** | N | N | N | N | Y | Y | N | Y | N | N | N | N | N | N |
| **Coma** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Lethargy** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Mortality** | N | N | N | N | N | N | N | N | N | N | N | N | N | N |

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**Supplement figure 1**: the cytotoxicity of root, bark, leave and fruits in cancer cells (MCF-7) and normal cells (L929).

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**Supplement figure** **2**: structure of the identified compounds.

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**Supplement figure** **3**: the cytotoxicity of PTX and BLEA in MCF-7 cells.

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**Supplement figure** **4**: Histological evaluation of toxicity of BLEA in different vital organs. HE staining was done to visualize the cellular architecture of different tissues of control and treated groups.

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**Supplement figure** **5**: Effective dose determination of BLEA using different doses (50, 100 and 200 mg/kg b. wt.) in comparison of control (pilot study).