week on, these parameters were back to control levels. The modulation of oxidative state of C57/B6 lung was not accompanied by histological modifications. Surprisingly, we did not observe the same results in the susceptible A/J mice.
In the present study, we have shown that urethane modulates redox components of the lung and this effect seems to be strain dependent. It is known that urethane-treated A/J mice will develop lung adenocarcinoma within 16−20 weeks after the first injection and that only a very small percentage of C57/B6 will develop lung cancer under the same conditions. Therefore, we put forward the idea that the ability of the resistant mice to up regulate a proper stress response at an initial stage act as a protective mechanism against carcinogenesis. On the other hand, the apparent lack of response observed in susceptible mice might mitigate the establishment of a chronic nocive environment that would contribute to the development of lung adenocarcinoma.

588 Aloe vera and honey solution decreases cell proliferation and increases apoptosis susceptibility in tumour tissue while avoids liver damage

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Background: Cancer is diagnosed in approximately 11 million people and is responsible for approximately 8 million deaths worldwide every year. Researches in cancer control have shown the importance of co-adjuvant therapies. *Aloe vera* may reduce tumour mass and metastasis rates, while honey may inhibit tumour growth.
Materials and Methods: This study verified the influence of *Aloe vera* and honey on tumour growth evolution accessing cell proliferation rate (Ki67-LI) and apoptosis susceptibility (Bax/Bcl-2 ratio) in tumour and liver tissue from adult rats at 7, 14 and 20 days of Walker 256 carcinoma (sc) implant. Tumour-bearing Wistar rats were distributed into two groups: *Aloe vera* and honey-treated group (WA) received a gavage with a 670 ml/kg dose of *Aloe vera* and honey solution daily, while non-treated group (CW) received only 0.9% NaCl solution in the same dose.
Results: The effect of *Aloe vera* and honey against tumour growth was observed through WA versus CW, showing decrease in tumour relative weights (CW-7d = 0.79±0.32; WA-7d = 0.68±0.43; CW-14d = 4.14±2.08; WA-14d = 3.17±1.38; CW-20d = 7.57±2.98; WA-20d = 5.16±2.46 (%)), lower cell proliferative rates (Ki-67 LI: CW-7d = 71.0±10.9; WA-7d = 51.4±18.1; CW-14d = 69.6±13.5; WA-14d = 37.2±16.4; CW-20d = 59.1±22.7; WA-20d = 32.0±3.3), and increase in apoptosis susceptibility (Bax/Bcl-2 ratio: CW-7d = 0.39±0.05; WA-7d = 2.35±0.08; CW-14d = 0.55±0.24; WA-14d = 2.48±2.16; CW-20d = 0.15±0.06; WA-20d = 1.20±0.80). In contrast, we observed that the *Aloe vera* and honey treatment leaded to increase in hepatocytes proliferation in early stages of tumour development (CW-7d = 12.6±3.3; WA-7d = 19.9±1.8; CW-14d = 7.2±1.4; WA-14d = 10.2±1.7; CW-20d = 10.9±1.8; WA-20d = 7.8±1.5) and decrease in their apoptosis susceptibility at 14th day of tumour implant (Bax/Bcl-2 ratio: CW-7d = 0.93±0.53; WA-7d = 0.86±0.62; CW-14d = 4.06±2.39; WA-14d = 0.88±0.63; CW-20d =3.53±3.24; WA-20d = 3.34±0.88), suggesting a possible protective effect in liver tissue, which is commonly harmed by tumour effects.
Conclusion: These data suggest that *Aloe vera* and honey affected tumour and host in a different way, inducing some benefits to host tissue while promoted damages in tumour evolution. Indeed, there are a large number of complex mechanisms involved in tumour growth, apoptosis and host health maintenance that can be modulated by *Aloe vera* and honey.

589 Extracts from endemic plant Helichrysum zivojini suppress survival of malignant cells

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Background: A wide variety of compounds and extracts from medicinal plants are in the center of attention of modern anticancer research as potential bioactive agents which might be used in future for the suppression of initiation, promotion and/or progression of malignant diseases. In this study our main goal was to investigate the anticancer properties of endemic plant species *Helichrysum zivojini* collected in Macedonia.
Material and Methods: The aerial parts of the plant were air-dried, powdered, and successively extracted with solvents of increasing polarity to obtain hexane, dichloromethane, ethyl-acetate, *n*-butanol and methanol extract. The cytotoxic activity of five obtained extracts was tested against selected cancer cell lines: human cervix adenocarcinoma HeLa, human breast adenocarcinoma MDA-MB-361, human malignant melanoma Fem-x, human myelogenous leukemia K562, unstimulated and stimulated for proliferation by phytohemagglutinin normal human immunocompetent peripheral blood mononuclear cells (PBMC) using MTT test. The mode of K562 cell death was analyzed morphologically.
Results: All investigated extracts exerted a selective dose-dependent cytotoxic action against all used target cancer cell lines and to PBMC stimulated for proliferation, but cytotoxic action was not as pronounced to normal, rested PBMC. The very prominent cytotoxic effect was observed against K562 cell line (IC_{50} values ranging from 11.78±0.94 to 74.88±7.57 μg/ml). Moreover, cytotoxicity of different extracts of *Helichrysum zivojini* was significantly stronger toward HeLa, Fem-x and K562 cancer cell lines than toward healthy immunocompetent PBMC stimulated for proliferation. It should be stressed that these extracts in whole exhibited weaker cytotoxic effect against unstimulated PBMC in comparison to stimulated PBMC. Morphological evaluation by microscopic examination of acridine orange and ethidium bromide stained K562 cells pre-treated for 48 h with plant extracts applied at a double $IC50_{72h}$ concentrations, demonstrated that all five extracts induced apoptotic cell death.
Conclusion: Results from this research show that extracts prepared from endemic plant species *Helichrysum zivojini* possess very pronounced anticancer potential, which could be attributed to the observed very selective antiproliferative and apoptotic effect, specially exerted to malignant cells.

590 Anticancer activity screening of Thai medicinal plants in human leukemic cell line MOLT-4

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Many phytochemicals have been proved to be a good candidate for anticancer drug. Eleven Thai plants were thus selected based on local usage for anticancer activity investigation. The 50% ethanol-water crude extract were prepared from *Rhus javanica* (stem), *Pinus kesiya* (branch), *Cratoxylum formosum* (stem), *Acorus tatarinowii* (leave & rhizome), *Tetracera loureirii* (vine), *Abrus pulchellus* (stem), *Catymbium speciosum* (rhizome), *Amomum villosum* (leave & rhizome), *Glochidion daltonii* (stem), *Rhus succedanea* (stem), and *Cladogynos orientalis* (arial part). The anticancer activity was determined from cytotoxicity and apoptosis induction in leukemic MOLT-4 cell and Vero cells. Cytotoxicity was tested by using Neutral red assay. An alkylation reaction with nitrobenzylpyridine (NBP), a nucleophilic DNA model was also examined. Apoptosis induction was evaluated from DNA fragmentation by using gel electrophoresis. Results showed that the plant that showed strong cytotoxic (IC_{50} < 100 μg/ml) and high selectivity (SI > 3.0) at 24 h and 48 h was *T. loureirii* (IC_{50} of 53.9±5.4 and 68.4±7.4 μg/ml, respectively). While *A. pulchellus*, and *P. kesiya* showed strong cytotoxic and high selectivity only at 48 h (IC_{50} of 71.7±4.2 μg/ml and 74.0±7.5 μg/ml, respectively). The plants that showed strong cytotoxic but less selectivity at 24 h and 48 h were *G. daltonii* (95.5±6.4 μg/ml and 61.0±3.9 μg/ml) and *C. speciosum* (99.4±3.6 μg/ml and 86.9±9.1 μg/ml). *C. formosum* possessed strong cytotoxicity (76.2±4.1 μg/ml) only at 48 h. Other crude extracts were found to be moderate cytotoxic (100 μg/ml ⩽ IC_{50} ⩽ 500 μg/ml) or inactive (IC_{50} > 500 μg/ml). The crude extracts illustrated different alkylating activity and only *A. tatarinowii* (leaves) showed no alkylating activity. The first 4 plants, *C. formosum, G. daltonii, R. succedanea, and T. loureirii*, showed high alkylating activity with 36, 22, 16, and 16% compared to melphalan, a positive control. Alkylating activity also indicated the presence of some electrophilic substance in the crude extract which alkylate with the nucleophilic site of NBP. Interestingly, almost of crude extract exhibited DNA ladder at 24 h except *T. loureirii*, *G. daltonii*, and *C. orientalis.* To be concluded, *A. pulchellus*, and *P. kesiya* showed high potential anticancer activity. While, the other plants that exhibited apoptosis induction were also of interest for further study. The active compound contributed to the activity and detailed mechanism of action will be further carried on.

591 Methylation of the mismatch repair genes in head and neck cancer

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Background: The Mismatch Repair System (MMR) plays a crucial role in the maintenance of genomic stability and increases the fidelity of DNA replication by eliminating mismatches which occur during the replication process. The MMR system incorporates several genes and has been conserved from procaryotes to eucaryotes. Aberrant methylation of the CpG islands at the promoter region of the genes is an epigenetic change that leads to transcriptional silencing of tumour suppressor genes. However, transcriptional silencing of the MMR genes in head and neck cancer has not been investigated throughly. In this study we investigated methylation of six MMR genes and the