5th BCNP Brazilian Conference on Natural Products
XXXI RESEM
Atibaia – SP – Brazil
ISBN: 978-85-66836-10-3
Oct. 26–29th 2015

INFLUENCE OF SOLVENT SELECTION ON ANTIPROLIFERATIVE ACTIVITY OF *MENTHA PIPERITA* AERIAL PARTS.

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Purpose of study: The genus *Mentha* (Lamiaceae) is one of the most complex genus in the plant kingdom because of spontaneous hybridization of its species. *M. piperita* popularly known as peppermint is a hybrid species originated in Europe and widely world cultivated [1]. Previous studies of our group showed that the dichloromethane extract of *M. piperita* aerial parts presented a promisor anticancer effect in *in vitro* and *in vivo* assays [2]. Considering one of twelve principles of green chemistry [3], the use of safer solvents, this study aimed the evaluation of the impact of dichloromethane replacement by sequential extraction with hexane and ethyl acetate, on antiproliferative effect of *M. piperita* aerial parts. **Methods and Results:** Freeze-drier milled aerial parts of *M. piperita* collected on CPQBA experimental field (May/2014) were extracted (1:3, m/v) by dynamic maceration (3 x 90 min) using two solvent schedules [dichloromethane (ED) and successively extraction with hexane (EH) and ethyl acetate (EEA)]. After complete solvent evaporation, the extraction yield (%, m/m) was calculated and extracts were evaluated by TLC (F.M.: CH_2Cl_2/CH_3OH 99:1, v/v). Successively extraction with hexane (1.37 %) and ethyl acetate (1.24%) afforded a quite similar yield that obtained to ED (1.24%) and TLC profile of EH was very similar to that observed for ED while EEA resulted in a more polar profile on TLC conditions. The antiproliferative activity was assessed in tumor [U251 (glioma), MCF7 (breast), NCI/ADR-Res (ovarian, multidrug resistant), 786-0 (kidney), NCI-H460 (lung, NSC), PC-3 (prostate) and HT-29 (colon)] cell lines exposed for 48 h to aliquots of ED, EH and EEA (0.25 - 250 μg/mL) and it was expressed as the concentration necessary to promote 50% of growth inhibition (GI_{50}). Considering mean $logGI_{50}$ values against tumor human cell lines, both ED (mean $logGI_{50}$ = 1.39) and EH (mean $logGI_{50}$ = 1.30) showed a similar cytostatic effect as expected by the chemical similarity observed on TLC analysis. Moreover, EEA (mean $logGI_{50}$ = 1.60) weakly inhibited tumor cells growth. **Conclusions:** These results pointed that the replacement of dichloromethane by hexane followed by ethyl acetate was a good strategy to obtain the compounds responsible for the antiproliferative effect presents in aerial parts of *Mentha piperita*. (FAPESP #2011/12394-8, #2011/14803-2, #2011/01114-4)

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