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The antiviral activity and mechanism of action of medicinal plants against herpes simplex virus type 1 (HSV-1)

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Many antiherpetic compounds currently in the clinical use have a narrow spectrum of activity, limited therapeutic usefulness and variable toxicity. There is also an emerging problem of resistant viral strains.

This study was undertaken to examine the anti-HSV-1 activity of some essential oils and their main constituents, monoterterpenes, phenylpropanoids and sesquiterpenes in vitro. All tested essential oils and most components exhibited high levels of antiviral activity against HSV-1. Essential oils were able to reduce viral infectivity by >90%, the monoterpenes inhibited HSV-1 by about >75%. Phenylpropanoids inhibited HSV-1 infectivity by 60-80% and sesquiterpenes constitutes by 40-98%. Star anise oil, β-caryophyllene, peppermint oil and tea tree oil showed highest selectivity index (ratio of TC_{50}/IC_{50}) for the cytotoxicity and plaque reduction assays of 160, 140, 64 and 60, respectively. These compounds seem to be preferable as potential agents against HSV-1. The mode of antiviral action has been determined, only minor antiviral effects were obserevd by essential oils and components when these drugs were added to host cells prior to infection or after entry of HSV-1 into cells. However, both essential oils and components exhibited high anti-HSV-1 activity by direct inactivation of free virus particles.

This report also demonstrates the antiviral activity of *Melissa officinalis* aqueous extract and its phenolic components named as, rosmarinic acid, caffeic acid and *p*-coumarinic acid against

HSV-1 in vitro. Melissa extract and *p*-coumarinic acid showed higher selectivity indices which indicating less toxicity and higher inhibitory effect than other compounds. The data presented in this report also indicated that melissa extract and its components are effective in inactivating HSV-1, when the virus was exposed before adsorption. No differences were detected in the plaque reduction assays when cells were treated with these components before HSV-1 adsorption or after infection. Meanwhile, treatment of cells with melissa extract before virus adsorption led to a high enhancement of inhibition as determined by a yield reduction assay of around 78% reduction. We found that attachment and penetration of HSV-1 to cells is inhibited by melissa extract. Other components, caffeic acid and *p*-coumaric acid were not effective to prevent virus attachment and penetration. In contrast, rosmarinic acid was effective to prevent viral attachment. There was no inhibition of two HSV-1 protein expression as determined for, ICP0 (an immediate early protein) and gD (a late protein). This indicates that viral replication was not inhibited at early steps by melissa extract and its components.

In conclusion, this study describes that essential oils, melissa extract and their components possess an anti-HSV-1 activity, which is likely revealed through direct inactivation of HSV-1. Further studies will be required to reveal the detailed antiviral mechanism of essential oils, melissa extract and their components.