The Janus Corner

This occasional section within the journal surveys visions and achievements, often not on the main track of the developing biomedical sciences, but all relating to discoveries and developments of medicinals–both ancient and modern. What they have in common, in one way or another, is providing further background and glances around the edges of the core discipline of pharmacognosy, as it has been and continues to evolve within our times.

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Original Article

Cistus incanus and *Pelargonium sidoides* extracts block enveloped viruses inluding HIV, Ebola and Marburg from entering human cells

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Recent studies have reported that extracts prepared from the medicinal plants *Cistus incanus* and *Pelargonium sidoides* prevent HIV from binding to human cells, thereby preventing it from those infecting cells.[1,2] The extracts were reported to inhibit a wide range of HIV-1 and HIV-2 clinical isolates, including a viral isolate which is resistant to all other drugs which are generally used as a part of normal anti-retroviral combinational therapies. The phytochemical extract compounds were found to target and bind to viral envelope proteins. The active compounds bind the cellular proteins and prevent them from interacting with host cell surface CD4 receptors. Of further interest, the research team also reported that the extracts not only blocked HIV cell entry, but had similar effects against both Ebola and Marburg viruses. The team speculated that the extracts may also have similar preventative effects against a wider range of enveloped viruses, included influenza viruses and therefore have broad medical implications. Notably, the study also trialled the extracts in long term studies to determine whether prolonged treatment would result in the development of viral resistance and reported no resistant viruses were found. The research has exciting implications. As the extracts have very different antiviral activities to all current clinical therapies, the extracts may be useful complementary therapies for the prevention and treatment of a wide range of viral diseases.

1. Rebensburg S, Helfer M, Schneider M, *et al*. Potent *in vitro* antiviral activity of *Cistus incanus* extract against HIV and Filoviruses targets viral envelope proteins. Scientific Reports. 2016;6:20394 DOI: 10.1038/srep20394
2. Helfer M, Koppensteiner H, Schneider M, et al. The root extract of the medicinal plant *Pelargonium sidoides* is a potent HIV-1 attachment Inhibitor. PLoS ONE. 2014;9(1):e87487 DOI: 10.1371/journal.pone.0087487

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A mushroom used in traditional Chinese medicine to promote health and longevity reduces weight in obese mice

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Ganoderma lucidum is a mushroom of the class Basidomycota which has a long history of use in Traditional Chinese Medicine (TCM) to promote health and longevity. Polysaccharides and triterpenoids from the *G. lucidum* fruiting body inhibit adipocyte differentiation and induce hypoglygemia and antihyperlipidemia in diabetic mice. However, despite these well characterised activities, no studies had previously examined the effects of *G. lucidum* on weight loss. A recent Tiawanese study has reported that aqueous *G. lucidum* extracts can reduce obesity in mice.[1] The study also reported that the extract functions via modulation of the gut microbiota. The gut microbiota consists of a complex milieu of bacteria which contribute to nutrient acquisition and the regulation of energy metabolism. An alteration in the gut microbiota balance can adversely affect an array of metabolic and physiological processes, including the development of obesity. It was postulated that an alteration in the gut microbial balance may result in dysbiosis, resulting in intestinal gram negative bacteria releasing lipopolysaccharide (LPS) into the bloodstream, resulting in insulin resistance and obesity. Aqueous *G. lucidum* extracts were shown to reverse gut dysbiosis, and also maintain the integrity of the gut barrier, effectively blocking LPS release in to the bloodstream and the downstream induction of obesity. Furthermore, the research identified *G. lucidum* high molecular weight polysaccharides as the prebiotic agents responsible for preventing dysbiosis and obesity related metabolic disorders.

1. Chang CJ, Lin CS, Lu CC *et al. Ganoderma lucidum* reduces obesity in mice by modulating the composition of the gut microbiota. Nature Communications. 2015;6.

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Are GM tomatoes the next superfood?

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Researchers at the John Innes Centre in the UK have developed a method of developing industrially relevant levels of the useful natural products resveratrol and genistein.[1] Resveratrol can extend lifespan and has a variety of therapeutically important functions including antioxidant effects, anti-inflammatory activity, immunosuppression and antibacterial effects (Figure 1). Thus resveratrol has potential in the treatment of chronic inflammatory diseases, cancer and numerous pathogenic illnesses. Similarly, the soybean compound, genistein has been reported to prevent steroid hormone related cancers including breast cancer.[3] The group has been able to engineer genes encoding for AtMYB12 protein and proteins involved in resveratrol and genistein synthetic pathways into tomato plants. As AtMYB12 protein activates several metabolic pathways, including those involved in resveratrol and genistein production, the aim was to test whether the plants produced increased levels of these phytochemicals. The resultant tomatoes were found to produce as high as 80 mg of these compounds per gram of dried weight. To put this in context, this means that ingesting a single one of these GM tomatoes would effectively provide the same level of resveratrol as in 50 bottles of red wine! Or the same amount of genistein as in 2.5 kg of tofu. This has obvious implications for industrial scale production of these therapeutic promising compounds and provides insights into methods to produce high levels of other phytochemicals in plants.

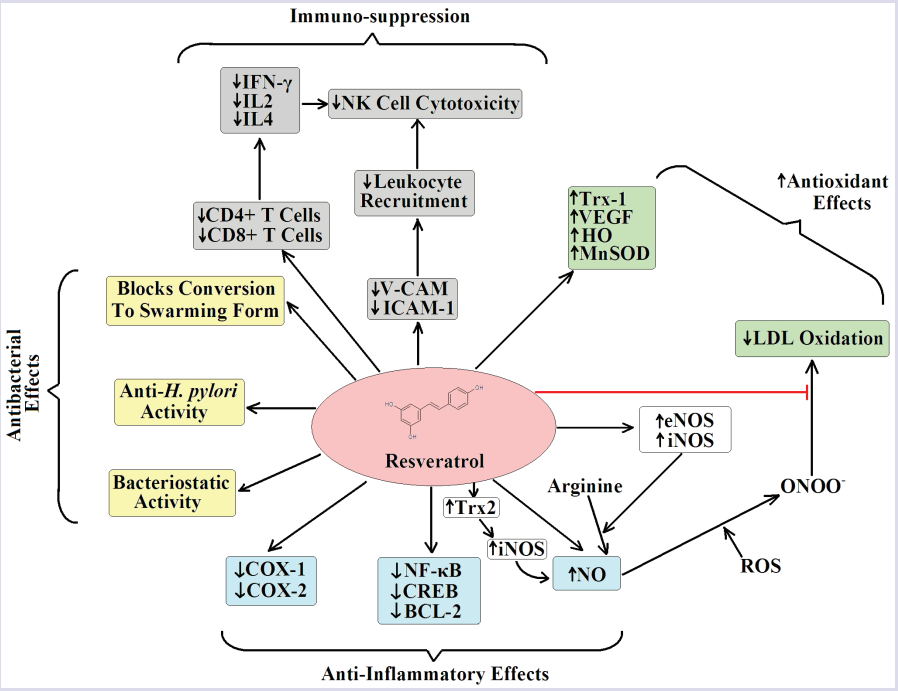

Figure 1: Known affects of resveratrol. Reproduced from[2] with author and publishers permission.

1. Zhang Yang, Butelli E, Alseekh S, *et al.* Multi-level engineering facilitates the production of phenylpropanoid compounds in tomato. Nature Communications 2015;6.
2. Cock IE. The early stages of rheumatoid arthritis: New targets for the development of combinational drug therapies. OA Arthritis. 2014;2(1):5.
3. Pagliacci MC, Smacchia M, Migliorati G, *et al.* Growth-inhibitory effects of the natural phyto-oestrogen genistein in MCF-7 human breast cancer cells. European Journal of Cancer. 1994;30(11):1675-82.