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### NEWS, VIEWS & REVIEWS

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Medical Marijuana: Where's the Data?

Bob Grant | June 30, 2014

With New York State poised to become the latest inductee into the legal medical marijuana club, The New York Times explored the science behind weed's effect on the variety of ills it's used to treat. The paper's verdict? Research into the medical benefits of smoked cannabis is severely lacking, and few findings point to a definitive therapeutic effect in the growing list of ailments that some physicians prescribe marijuana to treat, according to new laws. "I just don't think the evidence is there for these long lists," Molly Cooke, a professor of medicine at the University of California, San Francisco, told the Times. "It's been so hard to study marijuana. Policy makers are responding to thin data."

As The Scientist reported in 2012, many researchers who would like to study the medical effects of smoked marijuana are stymied by nearly insurmountable obstacles to securing both research-grade supplies of the drug and funding for clinical studies. A scientist wishing to conduct a rigorous trial of smoked marijuana on a particular human disease must first register with the Drug Enforcement Administration and file an investigational new drug application with the Food and Drug Administration, among other formalities. Once all these hurdles are cleared, researchers must still win funding, which is in short supply even for less-controversial work. "It's one thing to say we need to have more research, and it's another thing to obstruct the research," Steven Jenison, former medical director of New Mexico's medical cannabis program, told the Times.

This difficulty stems in part from marijuana's classification of an illegal, "Schedule I" drug as defined by the US Controlled Substances Act. According to that Act, the US government views cannabis—along with heroin and LSD—as a drug that has "no currently accepted medical use in treatment in the United States."

"The [cannabis] laws date to a time when what we knew about marijuana was voodoo," Mayo Clinic psychiatrist Michael Bostwick told The Scientist in 2012. "[The drug] can't be applied to humans and to therapeutics because the laws don't permit it to be done. The whole attitude towards medical marijuana is just irrational."

Evaluation Of A Highly Standardized Withania somnifera Extract on Endothelial Dysfunction and Biomarkers of Oxidative Stress In Patients With Type 2 Diabetes Mellitus: A Randomized, Double Blind, Placebo Controlled Study

Pingali Usharani et al

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Type 2 Diabetes mellitus is a multisystem disorder with oxidative stress and endothelial dysfunction. Withania somnifera Dunal (Ashwagandha) is shown to have potent antioxidant, hypoglycemic and hypolipidemic effects in several studies. The present study was planned to compare the effect of Withania somnifera on endothelial dysfunction and biomarkers in patients with diabetes mellitus. Materials and Methods: After taking IEC approval and written informed consent, 66 eligible patients, who are on metformin therapy, were randomized to receive either one capsule of highly standardized aqueous extract of Withania somnifera 250mg twice daily, one capsule of Withania somnifera 500mg twice daily or Placebo for a duration of 12 weeks. Primary efficacy parameter was a change in endothelial function (measured as change in reflection index of more than 6 %) performed by salbutamol challenge test at baseline and after 12 weeks of treatment. Secondary end points were change in biomarkers of oxidative stress (malondialdehyde, nitric oxide and glutathione), high sensitivity C-reactive protein and change in lipid profile. Safety lab parameters were measured, at baseline and after 12 weeks of treatment. Results: A total of 60 patients completed the study. Twelve weeks of treatment with Withania somnifera 250mg and 500mg produced significant reduction in reflection index ( $-2.52 \pm 1.32\%$  to  $-7.49 \pm 3.49\%$ ) and ( $-2.24 \pm 1.00\%$  to  $-9.03 \pm 2.42\%$ ) respectively, suggesting improvement in endothelial function versus placebo ( $-2.11 \pm 1.62\%$  to  $-0.81 \pm 2.86\%$ ). Similarly a significant improvement in biomarkers of oxidative stress, systemic inflammation, lipid parameters and HbA1c levels, compared to baseline and placebo, was observed with Withania somnifera. All treatments are well tolerated. Conclusion: Withania somnifera showed significant improvement in endothelial function, reduction in biomarkers of oxidative stress and systemic inflammation and can be used as a therapeutic adjunctive in patients with type 2 Diabetes mellitus

Effects of several quinones on insulin aggregation.

Gong, H. et al.

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Protein misfolding and aggregation are associated with more than twenty diseases, such as neurodegenerative diseases and metabolic diseases. The amyloid oligomers and fibrils may induce cell membrane disruption and lead to cell apoptosis. A great number of studies have focused on discovery of amyloid inhibitors which may prevent or treat amyloidosis diseases. Polyphenols have been extensively studied as a class of amyloid inhibitors, with several polyphenols under clinical trials as anti-neurodegenerative drugs. As oxidative intermediates of natural polyphenols, quinones widely exist in medicinal plants or food. In this study, we used insulin as an amyloid model to test the anti-amyloid effects of four simple quinones and four natural anthraquinone derivatives from rhubarb, a traditional herbal medicine used for treating Alzheimer's disease. Our results demonstrated that all eight quinones show inhibitory effects to different extent on insulin oligomerization, especially for 1,4-benzoquinone and 1,4-naphthoquinone. Significantly attenuated oligomerization, reduced amount of amyloid fibrils and reduced hemolysis levels were found after quinones treatments, indicating quinones may inhibit insulin from forming toxic oligomeric species. The results suggest a potential action of native anthraquinone derivatives in preventing protein misfolding diseases, the quinone skeleton may thus be further explored for designing effective anti-amyloidosis compounds.