



Wednesday, January 9, 2008

Dear Sir or Madam,

Evidence-based nutraceuticals, such as Glyrite, because of their pleiotropic properties, could well provide a critical missing link in contemporary diabetes care. It is cause for celebration when relatively non-harmful agents can be used by those seeking care for diabetes with its attendant complications.

Diabetes is a devastating disease that in the US accounts for the leading causes of adult blindness, non-accidental nerve disease and kidney failure, thus kidney dialysis and transplantation. Most diabetic patients die of cardiovascular disease (CVD) e.g. heart attacks, peripheral vascular disease and stroke which account for over 85% of deaths. Although the use of pharmaceutical prescription drugs have been shown to markedly reduce diabetic deaths due to CVD in a variety of global studies, it has been virtually impossible to significantly change the outcomes of CVD related to diabetes here in the US. For example, a recent study NHANES Study (2006) reported that the national HgbA1c level (a measure of body glucose control) has not changed in the last decade despite the above studies, and only 7% of patients have at least three of their CV risk factors at the guidelines recommended. There are a variety of well researched reasons for these facts. The main reasons are a) physician lack of training and willingness to use intensive methods for diabetes treatment, b) difficulty of patients obtaining medications in a too often dysfunctional health care system involving health care providers, government health systems at the national, state and local levels, c) insurance providers frequently unwilling to pay for drugs that save lives the most effectively and, d) lack of any form of health care access.

One way to circumvent these above problems is to get the above traditional health care delivery system out of the loop as the only source of care through the use of evidence-based nutraceuticals. These forms of treatments can be sold over the counter without the need for the often dysfunctional health care system. Several such products e.g. vitamins, trace minerals, cinnamon, garlic, ginseng and other products may be of some use. One group of products is flavonoids. Exceptional note is given to luteolin, a flavonoid that appears to have a variety of effects on diabetes in animal models, and in limited anecdotal human use.

Luteolin has been examined in several diabetic animal models. In the streptozotocin model, which results in the near total absence of insulin, e.g., that observed in type 1 diabetes, luteolin results in over a 20% reduction of blood glucose levels in the 20 day study, which increased to 50% if combined with a typical sulfonylurea drug commonly used in patients around the world. The latter drug had no significant effect when used alone. All the other indices of recovering diabetes in this model were also observed,



e.g., increased body weight, increased circulation insulin levels and increased cellular insulin production. Another animal model is the BB rat where both Type I and II diabetes can be evaluated. In the Type I model, "Glyrite", a product containing luteolin, was found to lower blood glucose levels by 31% acutely six hours after administration. In the Type II model, both acutely and after 20 days, glucoses were reduced by 28 and 41% respectively. The mechanisms of these effects are obscure, but some studies suggest the flavonoids e.g. luteolin inhibit alpha-glucosidase in the gut thus reducing glucose absorption into the blood. This kind of mechanism has been somewhat successful in human diabetic patients using prescription drugs, e.g. Glycet or Acarbose. Clearly other actions must be needed if these drugs work in Type I diabetic models, which is an autoimmune model that destroys the insulin producing islets. Other studies have shown that double negative T-cells are involved in the BB rat and NOD mouse models of Type I diabetes. These T-cells have potassium channels that are defective and further, these channels are altered by luteolin in a way to inhibit their actions.

Luteolin has received one or more US and international patents relative to its use in treatment of diabetes and related complications.

Finally, the flavonoids have been shown to interfere with another mechanism of diabetic complications unrelated to the direct effect of lower blood glucose, but rather to inhibit the toxic effects that glucose in high levels has on proteins to alter their natural state. This destructive process is known as glycation. The flavonoids inhibit glycation, even perhaps more strongly than aminoguanidine, a product tested in humans, but the latter was found to be too toxic. The flavonoids are natural occurring substances and tend not to be toxic in the amounts typically used.

In summary, nutraceuticals including luteolin, such as Glyrite, with their multi-factorial effects, deserve attention as a potentially new standard in diabetes care.

Sincerely,

M. Arthur Charles M.D., Ph.D.