Ascorbic acid (vitamin C) is a white crystalline compound that has high solubility in water (water-soluble vitamin). It has a strong reducing property; therefore it seems reasonable to expect that it functions metabolically in oxidation-reduction systems; as an antioxidant, protecting hydrogen carriers from destructive oxidation. Ascorbic acid has a role in tyrosine metabolism. It also appears to function in the conversion of folic to folinic acid. Vitamin C deficiency in humans has been known for centuries as scurvy. Many nutritionists believe that the human intake of ascorbic acid should be many times more than that intake level which produces deficiency symptoms. The daily value for ascorbic acid is 60 mg per day for non-pregnant women and the elderly have requirements up to 125 mg/day. Requirements for smokers are increased by as much as 40 percent. The normal plasma ascorbic acid concentrations are 60–80 mmol/l. [1-3]

Vitamin C is believed to play an important role in stress reactions, in infectious disease, and in wound healing. The role of ascorbic acid in infectious disease was reviewed by Hemila H. (1994), the review included 21 placebo-controlled studies which have been made to establish whether vitamin C at a dosage of > or = 1 g/day affects the common cold. The author could not find any consistent evidence in these studies to show that vitamin C supplementation reduces the incidence of the common cold (prevention of common cold) in the general population. However in each of the 21 studies, vitamin C reduced the duration of episodes and the severity of the symptoms of the common cold by an average of 23%. Although the results were with large variability in the gained benefits between the studies, in addition the author was unable to determine a clear clinical significance; however the consistency of the positive results in reducing the duration and severity of common cold episodes made him to conclude that the role of vitamin C use in common cold should be reconsidered. [4]

On an earlier review that was done in 1975 by Thomas Chalmers, the results of seven placebo-controlled studies were analyzed, in order to address the possible reduction in the duration of cold episodes with vitamin C use, reductions were only 0.11 +/-0.24 (SE) days shorter in the vitamin C groups which made the author conclude that there was no valid evidence to indicate that vitamin C (in doses 0.25-0.5 g) is beneficial in the treatment of the common cold.

Hemila et al; on the other hand had used data from the same studies that were reviewed by Chalmers, and they found that vitamin C but in higher doses (1-6 g/day) decreased the duration of the cold episodes by 0.93 +/- 0.22 (SE) days and the relative decrease in the episode duration was 21%. [5]

A Cochrane review by Douglas et al (2000), aimed at answering the following two questions:

1. Does regular high dosage supplementation with vitamin C reduce the incidence of colds?
2. Does taking vitamin C in high doses at the onset of a cold have a therapeutic effect?

The review included only published trials from two earlier published reviews by Kleijnen (1989) and Hemila (1992)
The FDA withdraws pergolide from the market and suspends tegaserod sales

At the end of March 2007 the FDA has notified health care professionals and patients that manufacturers and distributors of pergolide (Permax), have agreed to withdraw the drug from the market. Pergolide (dopamine agonist) which was indicated as adjunctive therapy to manage Parkinson’s disease had demonstrated in 2 new studies that some treated patients had serious damage to their heart valves compared with patients who did not take the medication, validating similar results that were obtained in earlier studies. Because the medicine should not stopped abruptly the FDA has advised patients who are currently taking pergolide to contact their health care professional about alternate treatments, while health care professionals were advised to evaluate their patients’ need for dopamine agonist (DA) therapy, and if continued DA treatment is warranted, another DA should be substituted for pergolide.

At almost the same time the FDA has announced that Novartis is suspending the US sales and marketing of its product Zelnorm (tegaserod maleate). The product is available in the Egyptian market under the name Zelmac® which is indicated for irritable bowel syndrome with constipation and chronic constipation. This decision was based on a recent retrospective analysis of data from more than 18,000 patients in which 13 of 11,614 patients treated with Zelnorm experienced cardiovascular-related adverse events (including myocardial infarction, stroke, and unstable angina pectoris) compared with 1 of 7,031 placebo-treated patients. However all affected patients had preexisting cardiovascular disease and/or cardiovascular risk factors.

Novartis and the FDA will discuss ways to keep Zelnorm available to appropriate patients.

Full details are available at http://www.fda.gov/
Cyanovirin; a new investigational drug with potential efficacy in Hepatitis C

The treatment of HCV has changed dramatically over the last decade, from controlling symptoms and complications to the ability to completely eradicate the virus. Management strategies can be divided into three main areas:

- Surveillance of patients with chronic HCV infection who have not developed cirrhosis.
- Surveillance of patients with established cirrhosis.
- Strategies to eradicate HCV. [1]

The two mainstays of treatment today are interferon and ribavirin. The combination of both drugs has resulted in marked improvements in sustained response rates: approximately 29% in genotype 1 patients and 65% in genotype 2/3; the response for genotype 4 which is widely spread in Egypt is similar to that of genotype 1. [2, 3] Therefore, there is a need for the development of additional therapeutic agents as many patients still are ineligible or unresponsive to current treatments. The genetic sequencing of HCV has allowed scientists to speculate on novel targets for antiviral therapy. Today protease inhibitors, helicases, and additional immunomodulatory agents are being studied for their potential effectiveness. [1]

Cyanovirin-N (CV-N) is a protein from the cyanobacterium Nostoc ellipsosporum (blue-green algae). This protein has the following characteristics: [4] It is 11-kDa protein, with primary amino acid structure that has no significant homology (less than 20%) to any known protein, and it shows a remarkable degree of stability and activity after exposure to drastic conditions such as:

- several freeze-thaw cycles.
- treatment with organic solvents (CH3CN, CH3OH, DMSO).
- denaturants (8M GnHCl).
- detergents (0.5% SDS), 0.5% H2O2.
- or even 15 min boiling.

In addition to being isolated from its natural source, CV-N was also expressed from recombinant DNA in Escherichia coli. The bioactivity of cyanovirin- N as highly potent virucidal agent has generated interest as a lead natural product for the prevention and therapy of human immunodeficiency virus infection. The mechanism of the antiviral activity of CV-N is mediated through specific, high-affinity interactions with the viral surface envelope glycoproteins; which render these glycoproteins incapable of mediating virus-to-cell or cell-to-cell fusion. It is well known that inhibition of viruses at the stage of viral entry provides a route for therapeutic intervention. [4, 5]

Non-HIV/AIDS-Related Uses; cyanovirin-N has potent in vitro activity against almost all strains of influenza A and B virus, moderate activity in vitro against some herpes viruses and is potentially active against some strains of hepatitis virus (bovine viral diarrhea virus) as a surrogate for hepatitis C virus (HCV). [4] In mouse models and in vitro, cyanovirin-N was active against the Zaire strain of the Ebola virus. [7]

The use of surrogate for HCV is due to difficulties in propagating the virus in cell culture, therefore, entry inhibitors have not yet been reported for this virus. However, with the development of retroviral particles pseudo-typed with HCV envelope glycoproteins (HCVpp) and the recent progress in amplification of HCV in cell culture (HCVcc), studying HCV entry is now possible. Helle et al (2006) has utilized this technology for the identification and the characterization of lectin cyanovirin-N in blocking HCV entry. [6] The rationale behind the use of CV-N in HCV in this study; is that the virus’ envelope glycoproteins are highly glycosylated, the target for which CV-N has high affinity. The authors found that CV-N inhibited the infectivity of HCVcc and HCVpp at low nanomolar concentrations. This inhibition is attributed to the interaction of CV-N with HCV envelope glycoproteins. In addition, the authors showed that the carbohydrate binding property of CV-N is involved in the anti-HCV activity. Finally, CV-N bound to HCV envelope glycoproteins and blocked the interaction between the envelope protein E2 and CD81, a cell surface molecule involved in HCV entry. Their data demonstrate that targeting the glycans of HCV envelope proteins is a promising approach in the development of antiviral therapies to combat HCV. [6]

The safety of CV-N has not been studied in humans, however cyanovirin-N appears to bind to viral oligosaccharides with high affinity and to mammalian oligosaccharides with low affinity, potentially providing potent inactivation of the virus and theoretically without potent adverse effects to the body. [8]

Conclusion

There is compelling need for a new therapy for HCV specially the more resistant genotypes 1 &4. CV-N initial results are promising to satisfy this need. The higher affinity of the drug to the viral glycoproteins than mammalian glycoproteins is initially reassuring about its safety, however the absence of safety data in humans makes its use restricted only to those who should benefit the most from the drug to outweigh the potential risk of adverse effects.

References:

Chocolate: Junk food or Healthy food?

In one study that was recently presented on March 2007 at the American College of Cardiology meeting in New Orleans; daily consumption of dark hot chocolate mix for six weeks was found to significantly improve the blood vessel flow of participants. The study which was a single blind placebo controlled, had involved 45 people with an average age of 52 and who were overweight. Participants were randomized to consume a Hershey dark chocolate mix (11 g of powdered cocoa mixed in eight ounces of water) with sugar (230 calories); a Hershey mix that was artificially sweetened (45 calories); and a placebo mix made of sweetened whey powder (250 calories) for six weeks, followed by a washout period of 4 weeks. Then a crossover was performed, whereas by the end of the study all participants had consumed each preparation for the same period (6 weeks). Daily sugar-free cocoa consumption improved flow mediated dilation (FMD) 2.4% over the study period and an eight-ounce cup of sweetened cocoa improved flow 1.5%, while placebo decreased flow mediated dilation by 0.8%. Although the results showed less effect by sugar containing chocolate than the artificially sweetened chocolate, it indicated an overall cardiovascular risk reduction by cocoa products. [1]

Dark chocolate & cocoa are rich sources in:

- Flavonoids
- Fiber
- Magnesium
- Arginine
- Caffeine
- Theobromine

Since ancient times, chocolate has long been used as a medicinal remedy. [2] However flavonoids (polyphenols) and cardiovascular health can only be traced back to epidemiological work performed about a decade ago. [3] It has been shown to improve endothelial function among healthy volunteers, elderly individuals, postmenopausal women, hypertensive patients, and others in small studies.

An inverse association between mortality from cardiovascular disease and daily intake of chocolate is now believed to be caused by the antioxidant flavonoids (including flavanols, catechins, epicatechins and procyanidins). The benefit was suggested to be via effects on lowering blood pressure, antiinflammation, anti-platelet function, higher HDL, decreased LDL oxidation. [4]

Conclusion:
There is multiple evidences from small randomized studies that suggest flavonoids to have possible protective effect against cardiovascular mortality; however, there is a need to conduct larger randomized trial to have definite beneficial effect of chocolate consumption on long-term cardiovascular outcomes before we can recommend it for this indication.

References:

1. Nijike VY, et al "Effects of Sustained Ingestion of Cocoa on Endothelial Function in Adults with BMI between 25-35 kg/m2: A Randomized, Single Blind, Placebo Controlled Trial" ACC meeting 2007; Abstract 1026-34.