

Stryer, 1988, *supra*). Cholesterol inserts into membrane lipid bilayers so that the hydrocarbon tail is located in the nonpolar core with the hydroxyl group bound to a carbonyl oxygen atom of a phospholipid polar head group oriented toward the aqueous exterior or interior of the cell (model 5 previous page). The interaction forces between sterol molecules seem to be little affected by the double bond in the ring system or modifications in the side chain. Also, the change in orientation of the hydroxyl group from 3-beta to 3-alpha does not significantly alter the cross-sectional area 10 of the sterol at the surface. However, replacement of the hydroxyl group by an oxogroup, or changes in the planar structure of the sterol nucleus, increase the molecular area, and may lead to some degree of membrane destabilization. This is why certain dimerized natural product plant components have antiparasite properties. Cholesterol prevents the crystallization of fatty acid chains by fitting between them. Thus, high concentrations of cholesterol tend to abolish phase transitions of lipid bilayers (Bloch, 1983, *CRC Critical Reviews in Biochemistry* 14, 47-92). Cholesterol (and sterol)—mediated stabilization from phase transitions of lipid bilayers is undoubtedly critical to the survival of Kintoplastida parasites which must undergo marked temperature transition from ambient (within the insect vector) to mammalian body temperature (37° C. or greater, dependent 25 on reservoir or human mammalian host) during their life cycle. Dependent upon T<sub>m</sub>, melting temperature, fatty acid acyl chains in bilayers can exist either a more rigid or ordered state favoring trans C—C bonds; or, at rising temperature, a more disordered or gauche C—C bond conformation (a 120-degree rotation, clockwise, g<sub>+</sub>, or counterclockwise, g<sub>-</sub>) increases. The transition temperature, T<sub>m</sub>, depends upon the length of the fatty acyl chains and amount of unsaturation. Saturated fatty acids result in an elevated T<sub>m</sub> (e.g. Crisco shortening, a solid at room temperature) whereas, greater unsaturation increases fluidity (e.g. vegetable oils, liquid at room temperature) lowering T<sub>m</sub>. Likewise, cholesterol prevents rigidity (crystallization) by fitting in between fatty acids increasing fluidity, so that at high membrane cholesterol concentrations, phase transition 40 of bilayers are largely abolished. An opposite effect of cholesterol is to sterically block large motions of fatty acyl chains, making membranes less fluid. Membrane fluidity, i.e. cholesterol content therefore, and indeed sterol content in general, has stringent biologic control for each cell type/function (Thompson, 1992, *The Regulation of Membrane Lipid Metabolism*, CRC Press, Ann Arbor).

Medicinal herbs are of considerable importance to the health of individuals and communities worldwide. Even in industrialized countries, an estimated 33% of the population use alternative treatments including herbal remedies. Approximately 35,000 to 70,000 plant species have been used for medical purposes (Zhang, 1996, *World Health 49th year* (2) :4-5). Given the extraordinary ratio (approaching 50%) of “active to total screened” plants developed from our ICBG ethnomedical and ethnobotanical “leads” for antiparasitics, one must be impressed by the accuracy of the traditional healers’ information. The fact that in the United States, two thirds of the drugs currently available on the market are originally based on medicinal plants then becomes somewhat less astounding (Micozzi, 1996, *World Health 49th year* (2):8-9). Most current antimalarials and other trypanosomals have their chemical origins in herbal extracts, thus, scientific history would lead one to believe that our ICBG approach is scientifically justified. The data 65 presented in this disclosure support the that conclusion that the herbal extracts which, in fact chemically resemble vari-

ous components of sterol biosynthesis and metabolism, act by inhibition of this pathway. The marked antiparasite efficacy of the known anticholesterol, antihyperlipidemics, cholesterol hormone antagonists, and anticancer drugs affecting this pathway for 3 of the four human parasite genera we have studied to date, not only provides immediate new chemotherapy for these infections in man and animals, but supports the concept that efficacious and nontoxic therapy for these diseases will be based on compounds affecting this pathway.

What is claimed is:

1. A method for treating an individual with a protozoan infection comprising administering to said individual a cholesterol synthesis inhibitor in a pharmaceutically effective amount, in a pharmaceutically effective excipient.

2. A method according to claim 1 wherein said administration is selected from the group consisting of oral, topical and parenteral.

3. A method as recited in claim 1, wherein said individual is a human.

4. A method for treating an individual with a protozoan infection comprising administering to said individual a cholesterol metabolism inhibitor in a pharmaceutically effective amount, in a pharmaceutically effective excipient.

5. A method according to claim 4 wherein said administration is selected from the group consisting of oral, topical and parenteral.

6. A method according to claim 4 where said individual is a human.

7. A method for treating an individual with a protozoan infection comprising administering to said individual a cholesterol excretion inhibitor in a pharmaceutically effective amount, in a pharmaceutically effective excipient.

8. A method according to claim 7 wherein said administration is selected from the group consisting of oral, topical and parenteral.

9. A method as recited in claim 7, wherein said individual is a human.

10. A method for preventing a protozoan infection in an animal comprising administering to said animal a cholesterol synthesis inhibitor in a pharmaceutically effective amount, in a pharmaceutically effective excipient.

11. A method according to claim 10 wherein said administration is selected from the group consisting of oral, topical and parenteral.

12. A method as recited in claim 10, wherein said animal is a human.

13. A method for preventing a protozoan infection in an animal comprising administering to said animal a cholesterol metabolism inhibitor in a pharmaceutically effective amount, in a pharmaceutically effective excipient.

14. A method according to claim 13 wherein said administration is selected from the group consisting of oral, topical and parenteral.

15. A method according to claim 3 where said animal is a human.

16. A method for preventing a protozoan infection in an animal comprising administering to said animal a cholesterol excretion inhibitor in a pharmaceutically effective amount, in a pharmaceutically effective excipient.

17. A method according to claim 16 wherein said administration is selected from the group consisting of oral, topical and parenteral.

18. A method as recited in claim 16, wherein said animal is a human.