2. There is no thorium in the ore, so the Pb-208 could not have come from decay of thorium.
3. Thus, the Pb-208 must have come from the addition of neutrons to Pb-207 atoms in the ore.

Having now gone back and checked some of the original sources of the data which Cook used, Heinze agrees with me that, "Pb-204 was indeed present in some of the Katanga ores." Thus, the first premise of Cook's argument is false, and his conclusion is unfounded. The Pb-208 in the ore is easily accounted for as due to the presence of common lead, and no appeal to fast neutrons is necessary or warranted. Cook simply misinterpreted the data table from which he was working.

This is the essential point; the remainder of Heinze's letter deals with relative inconsequentials. He is correct in asserting that: "Common lead" varies in composition from ore to ore." But this fact does not alter my point-the Pb-208 in these ores is found in the expected range of Pb-208/Pb-204 for common lead, and no appeal to fast neutrons is necessary or warranted in explaining its presence.

Heinze's statement: "Aardsma claimed to have checked the "original sources" of Cook's Katanga lead ore data" is not correct. (The same idea is repeated near the end of the letter.) I made no such claim. I tried to make the point that *Cook* obviously should have checked the original sources before making his claim regarding fast neutrons, and Heinze should have checked Cook's work, including the original sources, before asserting that "It can be said with confidence, however, that Cook's ratios demand accelerated decay in the past" (Heinze, 1992, p. 165), especially since both claims are so radical. I only needed to check a single original source to verify that Cook had misinterpreted the data table from which he had worked, and this is all I did. Since I explicitly stated "It was necessary [for me] to go back to at least one of the original sources for the Katanga data to be quite certain about what had been found in the Katanga ore" *(CRSQ* 29:105), and since I only referenced or referred to one original source in my letter, and since it would obviously be pointless to check all of the original sources when it was perfectly clear from reading just one that Cook had indeed misinterpreted the data table and his argument was thereby invalid, and since I nowhere claimed in my letter to have checked all of the original sources, I do not understand how Heinze made this mistake.

I am similarly at a loss to understand what logic led Heinze to his final remark: "Aardsma's claim that Cook misunderstood Nier's data appears to fall back on Aardsma himself." This remark seems totally out of place and incorrect to me.

I think Heinze's assertion that some of the Katanga ore samples would yield negative ages if corrected for primordial lead sounds interesting, though I do not immediately see how he arrives at this conclusion either. I encourage him to pursue this possibility, nonetheless, for a quantitatively and logically rigorous demonstration of this sort would obviously be of interest to many recent creationists, myself included.

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SOURCES AND APPLICATIONS OF BOTANICAL ALKALOIDS OFFER EVIDENCE OF CREATIVE PURPOSE AND DESIGN

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Abstract

Natural products phytochemistry, exemplified by the "bitter herbs," has served the medicinal needs of mankind since antiquity, and continues to do so in the present era. The appearance of pathogens resistant to existing pharmacology, notably to synthetic drugs, new diseases, and the continuing bane of cancers, cardiovascular diseases, endocrine dysfunctions, neurological disorders, immunopathology, etc. are stimulating renewed interest in possible biological sources of new therapeutic principles.

Remarkably, biogenic alkaloids having no direct function in the metabolism or structure of the plants that manufacture them have highly specific molecular interactions in man (or his infectious pathogens and/or their vectors) and the agents which plague his food sources. Such interactions underlie their pharmacological (or pesticidal) properties. These and related observations have significance to a creationist concept of their origin.

Introduction

In its quest for cures (and profits), the 20th century pharmaceutical industry has turned in large measure from natural sources to synthetic chemistry to provide our medicinal needs. Having thus progressed from the products and practices of arcane apothecary in our own culture, Western physicians of the present era tend to discount most of the natural "folk medicines" still employed in non-industrialized societies as superstitious palcebos, or of dubious therapeutic value, at best. [Critics maintain that such "medicinal" preparations packaged today for sale in health food stores, homeopathic and naturopathic "clinics," etc., typically contain quantities of potentially active ingredients too small to elicit pharmacological effects]. Attempts to incorporate them in modern medical practice are routinely branded as quackery. The National Council Against Health Fraud (comprised of some 2,300 physicians, scientists, and educators) is urging more stringent regulation of commercial herbal and homeopathic

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products otherwise that hint at health claims (Cote, 1993). Currently, most herbs, irrespective of their advertised or imputed applications, are considered food or food additives by the regulatory agencies; the majority of these products are, in terms of their realized health benefits, no more than expensive multivitamin tablets. Some, however, taken in unsupervised megadoses can produce undesirable side effects.

In the U.S., any substance that would be classifiable as a drug and so marketed as a medicine for use in the treatment of disease is subject to formidable evaluation by the Food and Drug Administration, and how it is used to continuing oversight by state medical boards. And justifiably—recall, for example, the controversy over Laetrile (originally a derivation from apricots) as a putative treatment for cancer (Kittler, 1963). Its efficacy to this application was eventually determined to be nil; the danger lay in the fact that many patients abandoned bona fide medical treatment for this vain hope of a cure. Thus, it is newsworthy when the shaman's crude balms, poultices and brews are discovered to contain, on occasion, potent antibiotic, anti-inflammatory, anti-tumorigenic and anti-pyretic (fever-breaking) principles, powerful analgesics, etc. Such research into folklore medicinals has nonetheless been sporadic, and regarded for the most part as time and cost inefficient. Still, it is not that long ago when in this country salicum—a preparation of white willow tree bark—was taken for the relief of headache; today, we reach for the synthetic acetyl salicyclic acid (aspirin), a nearly exact chemical replica of the natural medicine. If not any more efficacious, it is certainly more convenient.

However, faced with new diseases (e.g., AIDS) or ones newly characterized (e.g., Alzheimer's), and the challenges cancer, cardiovascular disease, diabetes, and an increasing number of drug-resistant strains of infectious pathogens [e.g., refractory tuberculosis (Beardsley, 1992) and malaria, below] continue to present, medical science is once again giving biology serious consideration as a source of "new" chemotherapeutic principles. As at least one authority has observed (Plotkin, quoted in Stix, 1993, p. 142), "Synthetics haven't proven to be the panacea." Since 1986, the National Cancer Institute has screened some 23,000 extracts from 7,000 plant species endogenous to the tropics. Several entrepreneurial ventures, with evocative names like Shaman Pharmaceuticals and Xenovia, have emerged during the last five years, along side such established concerns as Merck, Monsanto, Eli Lilly, Glaxo, Sandoz, and SmithKline Beecham, and the university-based institutes, where there has been a resurgence of interest and substantial investment in researching natural products pharmaceuticals. The effort is being glamorized not only by Hollywood (with Sean Connery in the role of a zealous botanist seeking the "silver bullet" cure for cancer in *Medicine Man),* but also by various activist "green groups" (e.g., Rainforest Alliance) who see the prospects of phytochemical resources as economic leverage to the mission of habitat conservation and the salvation of exotic biodiversity for its own sake (Joyce, 1992). Professional plant taxonomists, now calling themselves "ethobotanists," whose research for some time has been considered prosaic even by their academic colleagues, are finding increasing demand for their services in the biotechnology industry, as are those with doctoral degrees in pharmacognosy—the study of drugs from natural sources.

The fact of the matter is that plants and their natural products biochemistry have been serving man's medicinal needs since the Fall, as well as his nutritional needs since his creation. It has been said that a weed is only a plant for which a use has not yet been discovered. Thus has the Lord by His provision of the "bitter herbs" (referenced in Exodus 12: 1) blessed his human creation, even as it groans in its rebellion-inflicted travail.

Loosely defined, *alkaloids* are just that—"bitter herbs": pharmacologically active substances of complex and diverse organic chemical structure, characteristically bitter in taste and alkaline in reaction, found in the roots, leaves, bark, seeds, and other parts of a wide variety of plants. Alkaloids, as defined by their organic chemical properties, are also elaborated by some kinds of animals, but the discussion here will focus on those of botanical origin. [In some cases, zoological alkaloids may be acquired dietarily from primary botanical sources (see Williams et al., 1991)]. Typically, these compounds have no readily identifiable direct function for the plants that manufacture them, except as their toxicity and sharp unpleasant taste might provide a measure of defense against herbivores, parasites, and "pests" generally, or as their properties otherwise might serve to attract pollinating insects. Even so, considering the alkaloids as a whole, natural selection falls short as an explanation of their persistence and ubiquity.

Quinine and Malaria

The single most widespread disease of mankind, at present and historically, is malaria, manifested as a consequence of infection by protozoans of the genus *Plasmodium* (Figure 1). According to World Health Organization statistics, the current death rate is 1-2 million annually, the highest mortality being among children of sub-Saharan Africa (Ritter, 1992). It has been estimated (Zimmerman, 1960) that, cumulatively, half of the deaths in human history have been malaria-related. The impact of malaria on the history of the Old World has been reviewed by Sigerist (1970). Today there are more than 270 million people afflicted with malaria worldwide (Ritter, 1992), and over 1.4 billion people are living in areas where *Plasmodium* and the mosquitoes that transmit them *(Anopheles* spp.) also abide (Schmidt and Roberts, 1981). Extensive efforts are being made to develop an effective vaccine, but one suitable for wide scale use has yet to be obtained (Wyler, 1990; Gibbs, 1993). Epidemiological control measures continue to focus primarily on eradication of the mosquito vectors, and human infections are addressed pharmaceutically.

The ancient Chinese seem to have discovered the first antimalarial drug, represented by the Ch'ang shan herb and its alkaloid content (Schmidt and Roberts, 1981), but this remained obscure to Europeans until recently. On the other hand, the conquistadores discovered circa 1500 AD that the bark of *Cinchona* trees as brewed by the natives of South America is highly effective against malaria (also against amebiasis and several other endemic parasitic diseases that afflicted

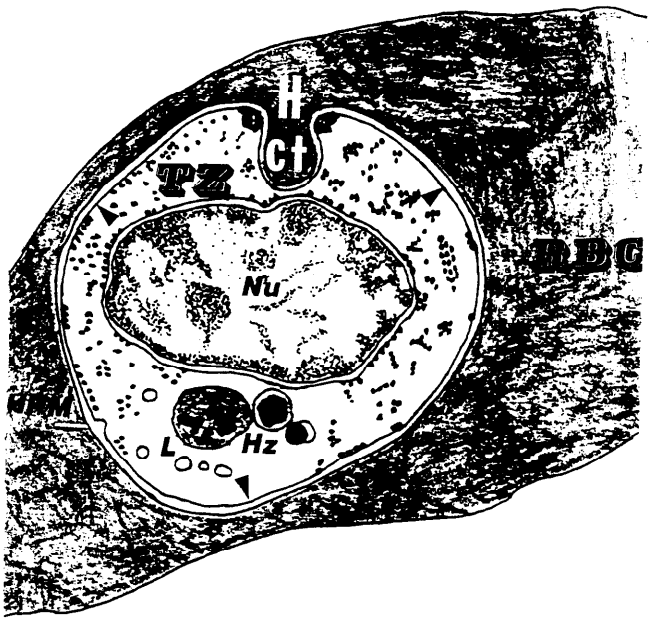

Figure 1. Drawing (from electron micrographs; see, e.g., Aikawa et al., 1966) of a malarial parasite *(Plasmodium* trophozoite, TZ; Nu, trophozoite nucleus) within its host erythrocyte (RBC). Its nutrition is derived largely from feeding on hemoglobin (H), ingested via the cytostome (Ct), and digested within lysosomes (L); at Hz, the dense, hemoglobin-derived pigment is being processed to the residual hemozoin crystalloid end product of hemoglobin digestion. This, apparently, is the site of the antimalarial action of the quinoline drugs quinine and chloroquine. The parasite's cell membrane (arrowheads) is the site in chloroquine-resistant strains of a transport mechanism for chloroquine efflux. Paralleling the parasite cell membrane is the host cell's plasma membrane-derived membrane (HPM) circumscribing the parasitophorous vacuole in which the parasite resides. See Aikawa (1971) for additional details of malarial parasite fine structure and host-parasite relationships.

the original inhabitants of the New World). The name honors a Countess Cinchona, who, on returning to Europe from Peru in 1640, formally introduced the remedy to civilized society. In exchange for this medical contribution to their culture, the Europeans introduced indigenous Americans—albeit with no malice aforethought—to such maladies as syphillis and pneumococcal pneumonia, viral poxes, perhaps cysticercosis taeniasis solium [i.e., the manifestation of infection with the so-called pork tapeworm, which remains a highly significant disease in Central and South America (see Flisser et al., 1982)], and imported African malaria with their slaves (see Zimmerman, 1980, and references therein). Fortuitously, the active principle in the cinchona brew—the alkaioid quinine—was effective against some of these pathogens as well.

Cinchona trees in their native South American habitats proved to be relatively inaccessible for obtaining large quantities of "fever bark" and with the European colonization of the Far East and Pacific, where malaria proved to be especially bothersome, *Cinchona calisaya/ C. ledgeriana* was transplanted by Dutch entrepreneurs to Indonesia for cultivation. Plantations in Java were especially productive. By the 1920's, the German pharmaceutical industry had perfected quinine's efficient extraction and, in the patent process, gained a monopoly on its international distribution. Then came World War II and the major sources of quinine were denied the Allies [Java fell to the Japanese in early 1942]. Anticipating the problems a shortage of quinine might raise, the U.S. military included on one of its last B-17 flights out of the soon to be lost Philippines a quantity of cinchona seeds, and new plantations were begun, ironically, in Central and South America. Even so, it was probably not lost upon the minds of military medicine that it would take awhile for the seeds to sprout and the trees (ergo bark) to grow. Meanwhile, the Allies all too soon (1942) found themselves conducting counterattacking military operations in the malaria infested jungles of New Guinea and the Solomons. In Papua, the U.S. Army's 41st division suffered a disabled by malaria ratio of 361 cases per 1,000 troops; on Guadalcanal, the ranks of the 1st Marine division were riddled more by malaria than Japanese ordnance, forcing its entire replacement; the much needed veteran 1st Marines did not fight again for a year (Morison, 1948, 1950; Luce and Billings, 1950).

As is often the case, necessity proved to be the mother of invention. A synthetic quinoline, chloroquine, developed by U.S. chemists in late 1941, was rushed into wholesale production and subsequently became the world's principal antimalarial drug. A variety of other synthetics used in conjunction with chloroquine increased the efficacy of malarial pharmacotherapy. Quinine per se faded into history. Man's creative genius had triumphed, it was said, over the caprice of nature and war's fortune. The eminent parasitologist Asa Chandler remarked in 1955 that ". . . (while) quinine remained the standard treatment for malaria for 300 years . . . it is still used only by physicians who have not kept up with the times" (p. 204).

Since the turn of the century, with knowledge of malaria's cause and transmission, the disease has been eradicated in most of the developed regions of the world. Post World War II, we have had the United Nations and its various proclamations of a new world order, and interests otherwise—politically, economically, and altruistically—in the underdeveloped sector, and a World Health Organization. With its new armamentarium of synthetic drugs coupled with the advent of DDT, the 1950's technology confidently predicted victory—globally—over the scourge of malaria. Professor Chandler (1955) wrote "Although there will be some areas in which malaria will continue to thrive for awhile Soper's estimate that 90 per cent of the malaria in the world can be wiped out by 1960 is not a pipe dream" (p. 209). According to Chandler, ". . . the slow process of evolution on which our parasitic enemies must depend is no match for the swift development of advantages afforded by human ingenuity" (1955, p. 2).

But there is a sequel to this story. During the 1960's, in the highlands of South Vietnam, the U. S. Marines discovered—again the hard way—an especially virulent strain of malaria, and something else. This *Plasmodium* variant was chloroquine *resistant* (Canfield, 1972). Other related synthetics in contemporary usage, e.g., amodiaquin, were likewise ineffective. For yet others, the "spread" between dosages effective against the parasites and significant patient toxicity was dangerously close, or for other reasons were contraindicated. Out of the desperation also born of necessity a supply of "obsolete" natural quinine was found, tried, and—it worked (Modell, 1968)! Ironically, among the scientists

suggesting this approach was Clark Read, who had obtained his Ph.D. under Asa Chandler's direction.

The antimalarial action of the quinoline alkaloids is apparently related to the process by which the intra-erythrocytic parasites (i.e., the stage living and multiplying in the red blood cells) sequester, and thereby render harmless, the digestion products of the hemoglobin on which they feed (Fitch, 1983; Slater and Cerami, 1992) (Figure 1). The drugs block one or more of the enzymes involved in the production of hemozoin crystals ("detoxified" ferriprotophorphyrin). The subsequent build-up of toxic heme residues kills the parasite. Parenthetically, it should be noted that this event is primarily therapeutic to the febrile paroxysms brought on by erythrocytic schizogony (multiplication of the parasites in the rbc's) and does not kill the non-hematophagous exo-erythrocytic (liver-dwelling) stages from which the erythrocytic form is derived. Therefore, to eliminate infection *in toto,* patients are concommitantly treated with other drugs effective against specific biochemical pathways in these stages [reviewed by Warhurst (1973) and Schmidt and Roberts (1981); see also Coatney (1976) for an insightful analysis of malarial relapse].

The chemical structures of quinine and chloroquine are provided in Figure 2, for comparison, since the differences underlie the mechanism for quinine's efficacy in the face of chloroquine resistance. In the chloroquine-resistant strains, there is a plasma membrane incorporated transport system which has a high affinity interaction with the molecular structure of chloroquine (vs. quinine) and pumps it out of the cell (Ginsberg et al., 1987). [The efflux of chloroquine by this carrier is probably a fortuitous coincidence (unless one chooses to believe that the parasite is designing a countermeasure to chloroquine therapy), but the function of this carrier in the parasite's physiology otherwise is yet unknown]. Therefore, these parasite cells do not accumulate enough chloroquine to inhibit heme processing. Absent a comparable efflux of quinine, however, quinine remains within and kills the chloroquine-resistant cells.

Strains resistant to synthetic antimalarials other than quinolines, e.g., the pyrimidine derivative pyrimethamine (Daraprim), have also been encountered. [In susceptible varieties, pyrimethamine is a selective inhibitor of *Plasmodium* dihydrofolate reductase (DHFR), an enzyme essential to the parasite's growth]. The basis for pyrimethamine-resistance has not yet been elucidated, though it may reflect the presence of a structural variant of *Plasmodium* DHFR (Wyler, 1990).

For a detailed, comprehensive technical treatise on alkaloid and other pharmacochemistry respective of malaria and other diseases of protozoan etiology, see Steck (1971).

Alkaloids have also played a significant role in the control and prevention of malaria and other insect-borne diseases as insecticides and repellants. Among the more potent naturally occurring compounds with this activity are the pyrethrins, from *Crysanthemum* flowers. Meanwhile, strains of anophiline mosquitoes resistant to DDT (the villain in Rachael Carlson's *Silent Spring)* and other synthetic insecticides have been encountered.

As evidenced by the current statistics, man's technology, its prognostications notwithstanding, has so far

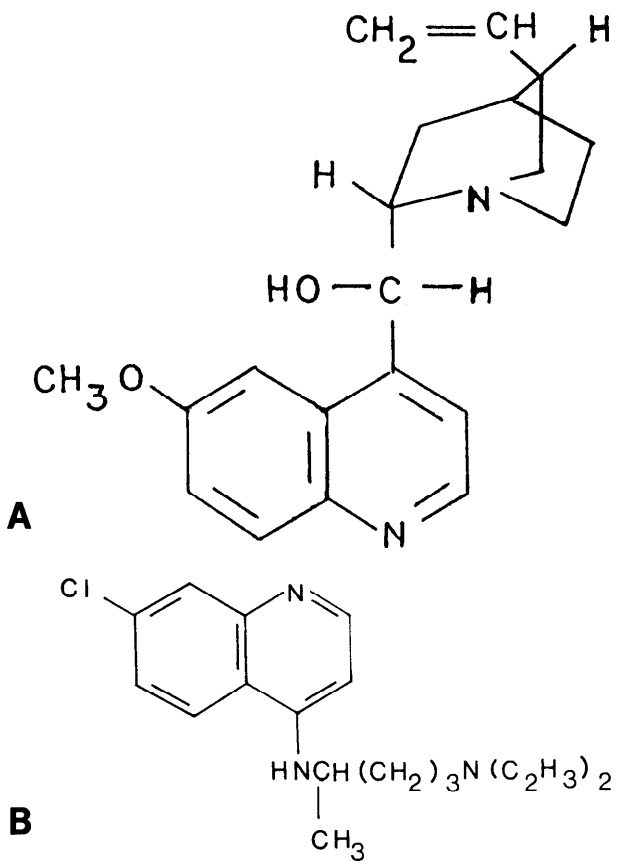

Figure 2. Molecular structure of two quinoline antimalarial drugs. A, the naturally occurring alkaloid, quinine. B, a synthetic version, chloroquine. From *The Merck Index,* eighth edition.

been inadequate to the cosmopolitan eradication of malaria. Schmidt and Roberts (1981), vs. Soper's earlier optimism (per Chandler, 1955), soberly reflect that ". . . known since antiquity . . ." (p. 141) "Malaria will be with us for a long time, probably as long as there are people" (p. 164).

Shedding little light on the problem or being productive to a solution is the prevailing establishment view that the parasites and their vectors are *evolving* drug resistance and insecticide tolerance, respectively. The term "acquired resistance" is, for the most part, misleading, since what is actually being observed is a statistical phenomenon applied to populations of organisms, not necessarily biological changes in the organisms themselves. Selection, as it may enhance changes in the composition of a population's structure, does not "create" biological characteristics *de novo* [for a critical review of the Cairns / Hall directed mutation hypothesis, see Lenski and Mittler, 1993]. Rather than "newly evolved (or evolving)" *Plasmodium* and *Anopheles* species, it seems clear from comparative biochemical studies (when these are interpreted without the evolutionary presumption) that the explanation lies in pre-existing genetics (i.e., already established variants) and / or inductive mechanisms analogous, e.g., to those of mammalian hepatocytes that underlie the expression of phenobarbital tolerance (Orrenius and Ericsson, 1966; Gillete et al., 1969). In the liver, barbituates (and other exotic toxins) are fortuitously rendered pharmacologically inactive by an oxidative hydroxylation en

zyme system otherwise devoted to processing nascent vitamins, endogenous hormones, etc. It increases quantitatively with increasing (or chronic) presentations of its substrates. Inductive mechanisms might include selective gene activation and quantitative modifiers respective of gene products, gene amplification (increase in gene copy number), and/or isoform diversity in gene products [for identification and discussion of these mechanisms as they apply to variation, see Li and Graur (1991); Lumsden et al. (1992); Lumsden and Lumsden (1992)]. This perspective might identify a target of opportunity in the rational development of future therapies and control efforts. A non-evolutionary explanation has already clarified one aspect of malarial epidemiology, pharmacodiversity and differential virulence—the infectivity for humans by certain *Plasmodium* species normally occurring in simians (Garnham, 1966; Coatney et al., 1971; Collins and Aikawa, 1977). Thus, in some cases, "new" strains are, in reality, "old" species in different surroundings. Not unpredictably, evolutionists (see, e.g., Mattingly, 1976) strain this observation as "evidence" for the evolution of human malarial parasites from those of simian ancestry (coevolving with their hosts, but this is a *non sequitur* in so far as the drug resistance problem is concerned.

Some Other Therapeutic Alkaloids

Botanical alkaloids have found widespread application in public health. A few examples of medicinal alkaloids are noted here [references to these, and the identification of others, can be found in various editions of the *Merck index* and *Physician's Desk Reference].* Also note that in addition to those developed as human medicines per se have been the alkaloids of significance to veterinary medicine (especially as antiparasitic drugs) and agriculture (as pesticides). Starvation, after all, is a disease of some consequence. Among the examples of alkaloids with this agronomical application is nicotine. The insecticidal use of nicotine amounts to over 500 tons annually in the U.S. alone. It is also used as an external parasiticide for large animals and poultry and as a veterinary antihelminthic. Some food plants, notably the "wild types" vs. their horticulturally developed variants, are invested with endogenous alkaloids that confer resistance to foraging insects and parasites.

Among the more remarkable, recently discovered naturally occurring insecticides is azadirachtin, from the neem tree (endogenous to India and Burma). Amazingly, its toxicity is selective for pest species (including mosquitoes and the desert locust), leaving pollinating insects (and vertebrates) unharmed (cf. DDT, etc.). Its mode of action is twofold: one fragment (decalin) disrupts the susceptible insects' growth and development; another (the hydroxy furan component) deters them from feeding (Aldhous, 1992) (Figure 3).

Extracts of the tropical vines *Chonodendron* and *Strychnos,* employed by Amazonians to augment their hunting and military prowess, have been adopted (as, e.g., tubocurarine) in contemporary surgery as a muscle relaxant. On the other hand, eserine, an alkaloid of *Physostigma* vines, is an antidote for curare poisoning; its modern medicinal uses include reducing intraocular tension in glaucoma and the management of myasthenia gravis (a progressively paralytic disease initially manifesting in the facial musculature). Atropine, from

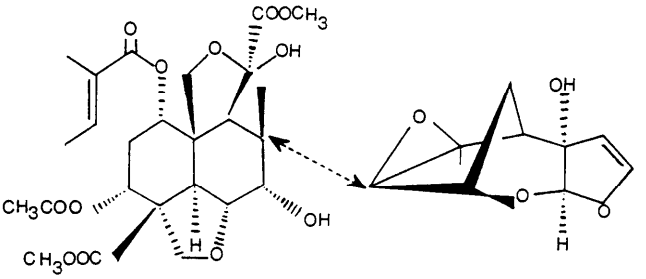

Figure 3. An alkaloid insecticide, azadirachtin, from the neem tree. At left, its decalin component; at right, its hydroxyfuran component. From Aldhous (1992).

Atropa belladonna (deadly nightshade), has a long history as a medicinal sedative (its nefarious Borgian applications notwithstanding) and antispasmodic. The latter property has had application to the treatment of cystitis, constrictive bronchial and esophageal spasms, and, in opthalmology, it is used as a mydriatic—i.e., to dilate the pupil of the eye; a recent application has been its use as an antidote to "nerve gas" poisoning. Historically more infamous, perhaps, is the conium alkaloid of hemlock, though in less than Socratic dosages it has had useful medicinal applications as an anodyne (pain reliever). Used for over two thousand years in India as a tranquilizer and treatment for snakebite, alkaloids produced by the *Rauwolfia* herbs were discovered by Western medicine in the 1930's and developed (as reserpine and its derivatives) for the pharmacotherapy of hypertension.

From antiquity, Chinese herbalists have employed a brew from the fruit, bark and wood of *Camptothecin acuminata* to shrink tumors. Its active principle, the alkaloid camptothecin, is the only known specific inhibitor of topoisomerase, the enzyme which uncoils DNA prior to its replication (Wang, 1985); camptothecin thereby blocks a mechanism essential to tumor cell proliferation. A semi-synthetic version of camptothecin (SmithKline's topotecan, which has lesser side effects) is presently in clinical trials (Stix, 1993), with encouraging results against no less than eight kinds of cancer. Spurred by reports that the rosy periwinkle *(Vinca rosea)* was being used in a folk treatment for diabetes in the Philippine hinterlands, Eli Lilly & Co. during the 1950's isolated the alkaloid vinblastin, which, while found ineffective for diabetes, has remarkable efficacy in the treatment of childhood lymphocytic leukemia (Joyce, 1992). Akin to the activity of the alkaloid colchicine (from meadow saffron, used in treating gout), vinblastin, at the level of molecular biology, inhibits microtubule polymerization, and thereby arrests cell division (Soifer, 1975; Salmon et al., 1984).

As reviewed by Stix (1993), at least three extracts from exotic plants have been discovered that exhibit activity against various facets of AIDS. One, from a yet taxonomically unclassified vine growing in the rain forests of Cameroon, inhibits replication of HIV (human immunodefficiency virus). Another, Calanolide A, from the Malaysian tree *Calophyllum lanigerum,* appears effective against an AZT (azidothymidine)-resistant form of HIV. A third, prostratin, from *Homolanthus nutans* (a plant species native to Samoa), appears to protect cells of the immune system from destruction by the AIDS-causing virus; for years,

Samoans have been using this preparation to treat yellow fever and other viral illnesses.

Besides their medical uses. alkaloids have been invaluable to cell biological research as highly selective inhibitors (antagonists) or activators (agonists) to functions associated with the cytoskeleton, membranes, the genome, etc. Colchicine and vinblastin, for example, have served as probes to elucidating the roles of microtubules; cytochalasin B to the diagnosis of activities involving actin-type microfilaments. The highly selective effects of certain alkaloids on ion-gating channels have provided stepwise analysis of the events involved with the generation of action potentials. Other alkaloids, e.g. forskolin, are specific agonists of adenyl cyclase; caffeine inhibits phosphodiesterase. Thus have the roles of cyclic nucleotides and related entities in a myriad of regulatory functions in cells been identified. Such basic research findings have had far ranging applications to our present understanding of cell structure and function, beyond those of pragmatic medical practice.

The Taxol Enigma

Another antimitotic alkaloid, taxol (which, cf. colchicine and vinblastin, inhibits microtubule *de-* polymerization), has proven remarkably effective in the treatment of lung, breast, and ovarian cancer (De Brabander, 1986). However, it takes over 10 tons of bark from the yew tree *(Taxus brevifolis)* to produce two pounds of taxol, and it requires 100 years or more for a Pacific yew to achieve a girth of just nine inches. Each potential patient (over 100,000 at present in the U.S. alone) would require the taxol contained in at least six trees per year.

Since the molecular structure of taxol has been elucidated (Figure 4). it would seem that chemists could solve the problem of scarcity by synthesizing the drug. However, to date, this task has proven greater than the efforts of the best laboratories in the world (Erickson, 1991; Amato, 1992). Among the alternatives to its industrial manufacture being explored is the *in vitro* cultivation of yew tree cells from which biosynthesized taxol might be harvested.

Chance Evolution or Creative Design?

Evolutionists tell us that the components of every organism, including the taxol in the yew tree—indeed, the yew tree itself—came about by processes originating in physicochemical randomness. This, they offer, explains the lack of specific function for many of the aforementioned alkaloids in the metabolism and structure of the plants in which they are found, overlooking at that point any purpose for which they might have been designed otherwise. Yet, in the case of taxol, such spontaneous molecular collocations have not yet been replicated in the orderly, purposeful investigations of our most competent chemists. The problem of synthesizing taxol, or a suitable derivative, may eventually be overcome, but it is doubtful that the pharmaceutical industry will resort to random chance in the process. More likely, it will require a great deal of intelligence, technology, and purpose aforethought. How, then, can these same chemists credit mindless evolution for the origin of this substance?

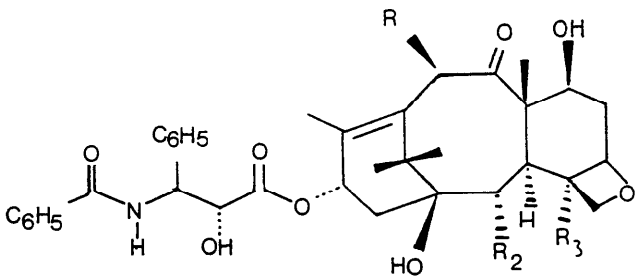

Figure 4. The yew tree alkaloid, taxol. From Amato (1992).

There are two general observations germane to the creationist concept of purpose and design in the context of the present topic. The first is that the synthetic drugs have been inspired by empirical experience with the natural products and elucidation of their structure. The synthetics are typically replicas of naturally occurring molecules or modifications to them. Thus, in the manufacture of topotecan, 10-hydroxyl-9-diethylamino methyl, is added to camptothecin per se to increase its water solubility and thereby improve its clinical use. Man's wisdom, or inventiveness, has not devised the structures of these drugs *de novo;* man has only learned, in some cases, how to assemble them. The point is that neither their structures nor their pharmacological activities are immediately predictable from brute organic chemistry.

The second concerns the highly specific effects *plant* alkaloids have on *animal* cells and the systems they constitute, systems that in many cases do not even exist in the plants themselves. A number, for example, are distinctly neurotropic. Moreover, there is the extraordinary stereospecific fit, ubiquitously, between medicinally significant alkaloids and molecular receptors (or structures otherwise, e.g., cytoskeletal tubulin) at these exogenous sites of their pharmacological activity. In some cases, an underlying commonality of chemical structure is suggested, particularly for those alkaloids having a substitutionary "first messenger" effect at receptors per se (Figure 5). This references the binding of a ligand to a cell surface receptor, which in turn is linked to regulatory enzymology (e.g., adenyl cyclase) or permeability (e.g., to Ca^{++}). See reviews by Snyder (1985) and Carafoli and Penniston (1985). Meanwhile, however, the receptors themselves, given their absolutely essential roles in the regulation of cell function, are otherwise structured to interact selectively with such endogenously produced, non-alkaloid ligands as biogenic amines, steroid and peptide hormones, neurotransmitters, kinins, prostaglandins, etc. Yet curare and atropine, endogenous to plants, bind specifically, as antagonists of the neurotransmitter acetylcholine at neuromuscular functions (hence their paralytic effect). [Acetylcholine, released from axon terminals, transiently binds to receptor channels in postsynaptic nerve and muscle cell membranes, generating a transmembrane, usually stimulatory, current flow. A spatially approximate enzyme, acetylcholine esterase, subsequently breaks down acetylcholine, stopping the signal. See review by Unwin (1989)]. Physostigmine (see eserine, above), from Calabar beans, is a specific inhibitor of acetylcholine esterase; this inhibition retards the regulatory decomposition of acetylcholine, enhancing the stimulatory effect of this neurotransmitter (hence eserine's anti-paralytic effect). *Rauwolfia-* produced alkaloids (see reserpine, above) act upon mechanisms which regulate indolamine (e.g., serotonin) and cate-

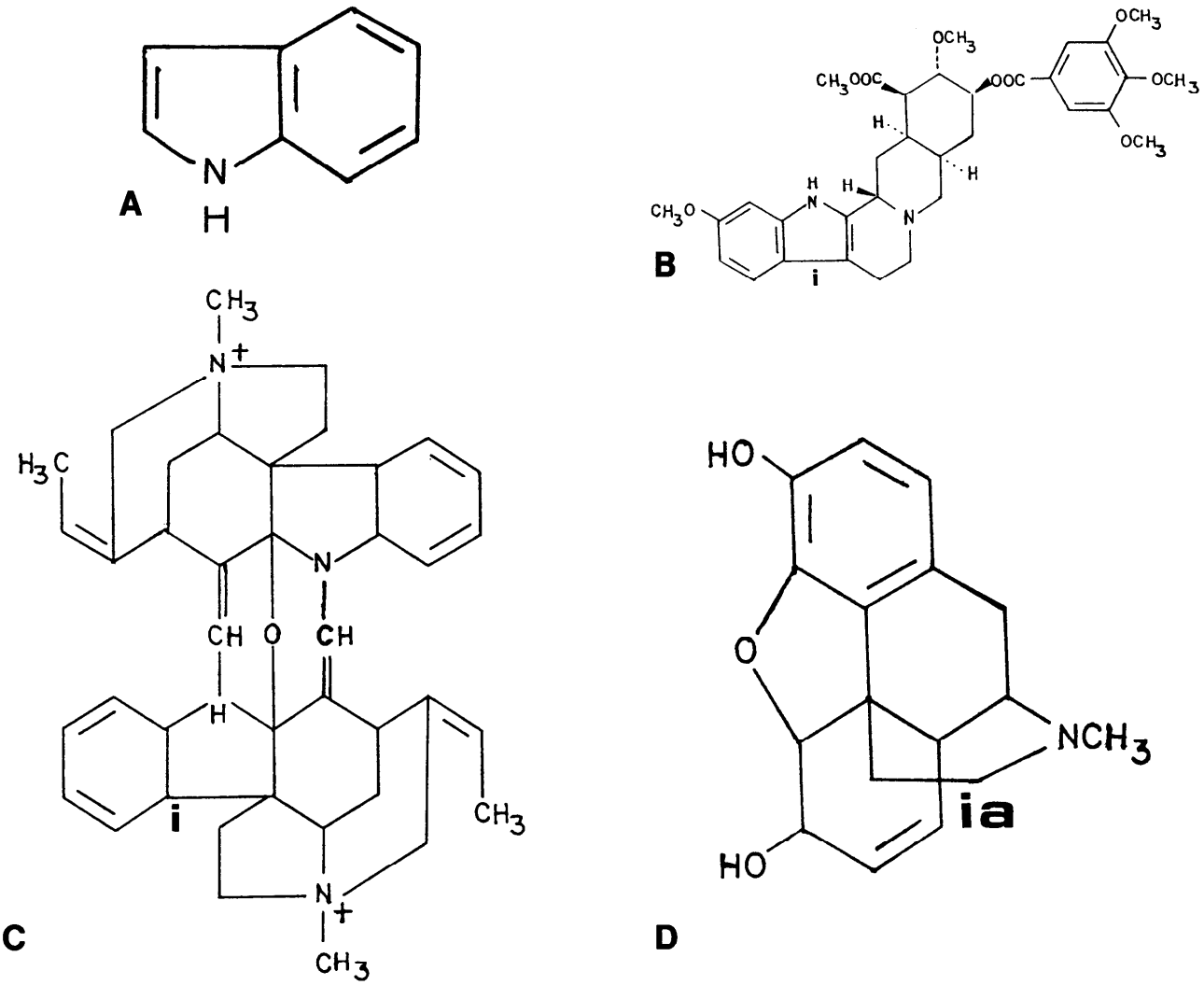

Figure 5. Receptor interactive botanical alkaloids frequently contain an indole structure (i) or analogue of it (ia) which may contribute to their affinity for sites on animal cell receptors and underlie their specific pharmacological activity as agonistically or antagonistically binding ligands. A, indole. B, reserpine. C, curare (C-curarine). D, morphine. From *The Merck Index,* eighth edition.

cholamine (e.g., adrenaline) concentrations in the mammalian central nervous system and peripheral tissues. Alkaloids produced in the seeds of certain poppy flowers *(Papaver somnifetum)* interact kinetically with the receptors otherwise responsive to the peptide analgesics—the endorphins and enkephalins (Snyder, 1977)—produced in mammals; hence the narcotic effect of opium and its derivatives. Quinine selectively blocks metabolic pathways unique to pathogenic microorganisms; i.e., the vulnerable "target" enzymology of the drug in *Plasmodium* trophozoites is non-existent in the parasite's human hosts. Meanwhile, quinine has no apparent function for the cinchona trees that manufacture it. And what natural principle would predict the effects plant alkaloids such as Calanolide A have against the AIDS virus? The selectively pesticidal activity of azadirachtin? These and the many additional examples which could be cited must strike the evolutionists as remarkable, if not inexplicable, "coincidences."

Ransom (1965, p. 117) finds that the

> secular economy is . . . inspired when science has found a process or tool that promises to win for mankind a fresh advantage from nature . . . It says nothing about God, who vanishes from the picture as soon as men think they see through nature.

What the secular economy is talking about in this instance is how the profits and rights to the "new" phytopharmaceuticals, as they might be discovered and exploited, should be distributed (Joyce, 1992); have we here negotiations among ". . . experts in greed—an accursed brood!" (2 Peter 2:14), who would eschew acknowledging the higher Source (and ultimate Owner) of the substances that would accrue to their good fortune? What royalties would He receive? Whom would the patents honor?

Thorns Among the Roses?

But there is an even darker side to the alkaloid story. Outwardly paradoxical to the creationist point of view would be that the medicinal efficacy of alkaloid drugs is often not without undesirable side effects. Many are frankly poisonous. If divinely created, why these "imperfections"? Of course, overt toxicity is often dosage related. Moreover, note that since the Fall, ". . . the

whole creation has been groaning . . . (Romans 8:22); see discussion by Morris (1988, pp. 124-128) of *devolutionary* changes and the development of disease itself, noxious elements, etc., respective of Genesis 3:17-18. A perhaps germane analogy in principle to this point is the example of hemorrhagic poisoning evidenced by cattle that have fed on silage contaminated with sweet clover. Cattle eating freshly cut clover or pasturing in fields in which it is growing do not develop sweet clover poisoning. The cause is a *decay* product, the anticoagulant dicoumarin, which is formed during the spoilage process from the harmless coumarins in fresh clover. Then there is the question raised by Williams et al. (1991) concerning various overt defense mechanisms (many of which employ alkaloids) evidenced by present day organisms: were some created as such, i.e., prior to the Fall? If so, what would have been their purpose to a perfectly harmonious creation?

Further potential rebuttal: why would a caring God have created addictive narcotics, for example? Where is the altruistic principle in that? The skeptic would point out that a crack cocaine addict, or her unborn child, is hardly blessed in that event. But *God* is not the cause of that unhappy circumstance, some exegeses of Genesis 3:18 notwithstanding (again, see Morris, 1988). Need we be reminded of *man's* ability, by his own volition and perverse ingenuity, to corrupt God's gifts? Even Christians who would abstain from alcohol, tobacco, and the non-prescribed use of drugs are not immune from this principle, as the incidence of dietary abuse—manifested in overweight, hypercholesterolemia, etc., and their morbid sequellae (Lumsden and Allen, 1992)—would attest.

Cocaine is an alkaloid originally employed productively as a topical anesthetic; the street drug heroin is aberrantly derived from the same family of alkaloids that have given us the medically legitimate analgesics morphine and codeine, papaverine (used as a smooth muscle relaxant and in the treatment of tinnitus), and noscapine (an antitussive, or cough remedy). The nicotine alkaloid has had application historically, as tobacco poultices, to the succor of rheumatic diseases; tobacco need not always have been a source of self-inflicted carcinogens inhaled in pipe, cigar or cigarette smoke. As noted above, nicotine is otherwise widely used today, beneficially, as an agricultural insecticide and veterinary antihelminthic. Its oxidation product, nicotinic acid, is, by the way, a natural constituent, albeit in usually minute amounts, of all living cells. Appreciable amounts are found in milk, white meat, liver, alfalfa, legumes, whole cereals, and corn. The nicotinamide derivative is, of course, otherwise known as vitamin B_3.

Where God-given resources are concerned, physical as well as spiritual, man would perish for a lack of knowledge, though it is there for anyone who seeks Him. Where ignorance has combined with pride, the results have been disastrous for mankind. Henry Morris summarizes man's plight in the title to one of his books, *The Long War Against God.* Where the particular topic of this paper is concerned, better we appreciate that God, (not evolution) gave every plant to use for our good (Genesis 1:29; 8-9). We should see His nature in what He has made (Romans 1:20), and for all things give thanks (Psalm 107; I Thessalonians 5:18)

This leads me to a final observation. The power of prayer, as it would call upon God's power, is man's greatest resource in the face of adversity. There is abundant contemporary testimony that He does in fact directly intervened on occasion, to relieve physical suffering and in the physical healing and curative processes. However, the view some take of secular medicine—as a compromise of one's faith—misses the point of the above discussion. God, as He created these medicinal principles (presciently?), provided them for our well-being, is not honored by eschewing them. Would a parent or guardian, who in naming and claiming a faith healing of his sick child and thereby forbids medical treatment, be tempting God? While man does not live by bread alone, he does not do very well without the bread either. The Lord provided manna—a physical substance—to sustain the Israelites—physically—during their 40 years sojurn in the wilderness. Given the state of the world today, are we not still lost in a wilderness, but yet still blessed by God's provisions? Let us praise Him, giving thanks in *all* circumstances.

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OTA BENGA: THE STORY OF THE PYGMY ON DISPLAY IN A ZOO

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Abstract

One of the most fascinating historical accounts about the fallout of biological evolution theory on human relations is the story of Ota Benga, a pygmy who was put on display in an American zoo as an example of an evolutionarily inferior race. The incident clearly reveals the racism of evolutionary theory and the extent that the theory gripped the hearts and minds of scientists and journalists in the late 1800s. As humans move away from this time in history, we can more objectively look back at the horrors that evolutionary theory has brought to society of which this story is a poignant example.

Introduction

Genetic differences are imperative to the theory of naturalistic evolution because they are the only source of innovation for evolutionary advancement. History and tradition has, often with tragic consequences, grouped human phenotypes that result from genotypic variations together into categories now called races. Races function as evolutionary selection units that are of such major importance that the subtitle of Darwin's classic 1859 book, *The Origin of Species,* was "the preservation of superior races." This work was critical in establishing the importance of the race fitness idea, and especially the "survival of the fittest" concept in evolution. The question being asked in the early 1900s was:

> Who was, [and] who wasn't human? It was a big question in turn-of-the-century Europe and America . . . The Europeans . . . were asking and answering it about Pygmies. . . . often influenced by the current interpretations of Darwinism, so it was not simply who was *human,* but who was *more* human, and finally, who was the *most* human, that concerned them (Bradford and Blume, 1992, p. 29).

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