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PHARMACY AND NATURE - PLENTY OF DIVERSITY

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In the most general sense, nature represents the unity of soil, water and air and all living beings. Man and all his activities affect life on our planet in different ways, often through gross violations of natural laws and fine, subtle connections and mutual influences of the environment and different species and forms of the living world. Numerous initiatives over the last decades indicate that every human activity and "world of people" should be observed, estimated and evaluated from the aspect of environmental impact. The development of the economy and society as a whole must be based on technologies that are in harmony with nature and that use natural resources in an organized and controlled manner that does not lead to devastation, violation of natural laws, and environmental disasters.

In the areas of health, preservation and improvement of the health of individuals and society, nature is important not only as a source of pharmaceutically active and auxiliary substances, but also as a source of ideas, problems and solutions that are hidden somewhere, and usually simple, but should be discovered and understood. From the idea of a pharmaceutical product, through the development of materials and technologies for their production, analysis and control, application in different patient populations, to the proper disposal and destruction of used and unused materials and products, everything is connected and has an impact on land, water and air, as well as to all living beings on this planet. In the scientific and research sense, but also through the professional aspect of pharmacy, pharmacognosy is most often associated with nature, as the main source of natural medicinal products.

In recent decades, pharmacognosy, as a concept and as a scientific discipline within the pharmaceutical sciences, has changed its focus. From the applied, descriptive botanical science, from the sixties of the last century, it moved to the chemical, biochemical and economic aspects of natural products (drugs) and their ingredients. And then in the 21st century, it becomes "a science that focuses on the study of the relationship between the structure and activity of ingredients, the therapeutic and use potential that natural products (drugs) have because of the ingredients they contain." Scientific pharmacognosy, today, should also include concrete assistance to herbal medicine manufacturers to provide safe and effective products; through research into bioavailability, bioequivalence, through standardization and quality control, but also through proper design of pharmaceutical forms and clinical studies to examine the efficacy of these medicinal products. Also, due to the growing number of different kind of products on the market, whose application is based on the presence of secondary metabolites of plants, it is necessary for pharmacists to be able to essentially understand those products, in proper, quality and safe way to produce, control and recommend them to users (1,2,3).

Fundamental research within pharmacognosy still aims to use the biological diversity of plants, algae, mosses, fungi, animals and microorganisms (on land and in the aquatic environment) to discover new compounds with some pharmacological activities. Diversity in

nature is not only seen through the number of living organisms. The diversity of chemically pharmacologically active structures, isolated from natural organisms, is very significant. According to certain authors, these compounds have more numerous and complex steric structures in relation to those obtained by organic synthesis. There are about 30,000 of them in the databases; about 13% were isolated from animals, 33% from bacteria, 26% from fungi, and 27% from plants (1).

We are still looking for medicinal substances that will prevent the growth of malignant cells, which will prevent or cure inflammatory processes, prevent and cure infection caused by pathogenic microorganisms, and affect neurodegenerative changes. Isolated compounds are used as such, their structure is partially changed or they serve as a model of a substance for the synthesis of completely new medicinal compounds. Here are described several examples of drugs whose active components originate from plants or have partially altered structures (acarbose, artemeter, docetaxel, paclitaxel, galantamine, camptothecin-irinotecan-topotecan...) (1). Prostratin (*Homolanthus nutans*, Euphorbiaceae), resveratrol, huperzine A, as well as artemisinin or betulinic acid are still the subject of clinical trials.

Also, herbal extracts are still being studied as active ingredients of herbal medicines, which achieve effects through the synergism of their ingredients. Researchers in the field of natural products are also engaged in current research on the use of waste materials to create new useful products and more complete use of biomass. In the presentation itself, different approaches to the research of natural medicinal products will be explained and documented in more detail.

It should also be emphasized that the largest amount of plant raw material for the isolation of compounds or the production of extracts is now produced by field production; production by fermentation of microorganisms is also used, and very rarely in bioreactors using cell cultures (taxol and ginseng biomass, for example). Equipment and technology are available, but problems arise regarding the price of the products obtained in this way.

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FARMACIJA I PRIRODA – BOGATSTVO DIVERZITETA

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Naopštije posmatrano, priroda predstavlja jedinstvo zemljišta, vode i vazduha i svih živih bića. Čovek i sve njegove aktivnosti utiču na život na našoj planeti na različite načine, često kroz grubo narušavanje prirodnih zakonitosti i fine, suptilne povezanosti i međusobnih uticaja sredine i različitih vrsta i oblika živog sveta. Brojne inicijative u toku poslednjih decenija ukazuju da svaka aktivnost čoveka i "sveta ljudi" treba da se posmatra, procenjuje i vrednuje i sa aspekta uticaja na životnu sredinu. Razvoj ekonomije i društva u celini mora biti zasnovan na tehnologijama koje su u saglasju sa prirodom i koje prirodne resurse koriste na organizovan i kontrolisan način koji ne dovodi do devastiranja, narušavanja prirodnih zakonitosti i ekoloških katastrofa.

Za oblast zdravstva, očuvanje i unapređenje zdravlja pojedinca i društva, priroda je važna ne samo kao izvor farmaceutski aktivnih i pomoćnih supstanci, već i kao izvor ideja, problema i rešenja koja su negde skrivena, i najčešće jednostavna, ali ih treba otkriti i razumeti. Od ideje za farmaceutski proizvod, preko razvoja materijala i tehnologija za njihovu proizvodnju, analizu i kontrolu, primene kod različitih populacija pacijenata, do pravilnog odlaganja i uništavanja iskorišćenog i neiskorišćenog materijala i proizvoda, sve je povezano i ima uticaj na zemlju, vodu i vazduh, kao i na sva živa bića na ovoj planeti. U naučnom i istraživačkom smislu, ali i kroz profesionalni aspekt farmacije, farmakognozija se najčešće povezuje sa prirodom, kao glavnim izvorom prirodnih lekovitih proizvoda.

Poslednjih decenija, farmakognozija, kao pojam i kao naučna disciplina u okviru farmaceutskih nauka, menja svoje težište. Od primenjene, deskriptive botaničke nauke, od šezdesetih godina prošlog veka, pomerala se ka hemijskim, biohemijskim i ekonomskim aspektima prirodnih proizvoda (droga) i njihovih sastojaka. A onda u 21. veku postaje „nauka koja u centru interesovanja ima proučavanje odnosa strukture i aktivnosti sastojaka, terapijskog i upotrebno potencijala koji imaju prirodni proizvodi (droge) zbog sastojaka koje sadrže“. Naučna farmakognozija, danas, treba da obuhvati i konkretnu pomoć proizvođačima biljnih lekova za obezbeđivanje sigurnih i efikasnih proizvoda; kroz istraživanje biorasplošivosti, bioekvivalencije, kroz standardizaciju i kontrolu kvaliteta, ali i kroz pravilno dizajniranje farmaceutskih oblika i kliničkih studije za ispitivanje efikasnosti ovih lekovitih proizvoda. Takođe, zbog sve većeg broja različitih proizvoda na tržištu, čija je primena zasnovana na prisustvu sekundarnih metabolita biljaka, neophodno je da farmaceuti budu osposobljeni da ove proizvode suštinski razumeju, na pravilan, kvalitetan i bezbedan način proizvedu, kontrolišu, preporuče korisnicima (1,2,3).

Fundamentalna istraživanja u okviru farmakognozije i dalje imaju cilj da biološku raznovrsnost biljaka, algi, mahovina, gljiva, životinja i mikroorganizama (na kopnu i u vodenoj sredini) iskoriste da otkriju nova jedinjenja, nosioce određenih farmakoloških aktivnosti. Diverzitet u prirodi se ne sagledava samo kroz broj živih organizama. Veoma je značajan diverzitet hemijskih farmakološki aktivnih struktura, izolovanih iz prirodnih organizama. Po određenim autorima, ove jedinjenja su brojnija i kompleksnije sterne strukture u odnosu na ona dobijena organskom sintezom. U bazama podataka ima ih oko 30000; oko 13% je izolovano iz životinja, 33% iz bakterija, 26 % iz gljiva i 27 % iz biljaka (1).

I dalje se traga za lekovitim supstancama koje će sprečiti rast malignih ćelija, koje će sprečiti ili izlečiti procese inflamacije, onemogućiti i izlečiti infekciju patogenim

mikroorganizmima i uticati na neurodegenerativne promene. Izolovana jedinjenja se koriste kao takva, delimično im se menja struktura ili služe kao model supstance za sintezu sasvim novih lekovitih jedinjenja. Ovde je dato nekoliko primera lekova čije aktivne komponente vode poreklo od biljaka ili su delimično izmenjene strukture (akarbosa, artemeter, docetaksel, paklitaksel, galantamin, kamptotecin-irinotekan, topotekan...) (1). Prostratin (*Homolanthus nutans*, Euphorbiaceae), resveratrol, huperzin A, kao i artemisinin ili betulinska kiselina i dalje su predmet kliničkih ispitivanja.

Takođe, i dalje se proučavaju biljni ekstrakti, kao aktivni sastojci biljnih lekova, koji efekte ostvaruju kroz sinergizam svojih sastojaka. Istraživači u oblasti prirodnih proizvoda, bave se i aktuelnim istraživanja iskorišćenja otpadnih materijala za stvaranje novih korisnih proizvoda i potpunije korišćenje biomase. U samom izlaganju, različiti pristupi istraživanja prirodnih lekovitih proizvoda će biti detaljnije objašnjeni i dokumentovani.

Treba, takođe, naglasiti da se najveća količina biljne sirovine za izolaciju jedinjenja ili izradu ekstrakata, danas proizvodi ratarskom proizvodnjom; koristi se i proizvodnja fermentacijom mikroorganizama, a sasvim retko u bioreaktorima korišćenjem ćelijskih kultura (taksol i biomasa žen-šena, npr.). Oprema i tehnologija su dostupne, ali problemi se javljaju kod cene ovako dobijenih proizvoda.

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