DTI
Drug Target Insights 2023; 17: 1-4
ISSN 1177-3928 | DOI: 10.33393/dti.2023.2548
EDITORIAL

Natural Products & Phytotherapeutics: why a new section?

Marcello Iriti

Department of Biomedical, Surgical and Dental Sciences, Università degli Studi di Milano, Milan - Italy

According to one of the most authoritative reports focusing on natural products as sources of new drugs, the use of natural products and their synthetic derivatives is still pivotal in the discovery of new drugs (1). Indeed, among the new drugs approved (N = 1881) in the last four decades, about 25% are natural products (Fig. 1A). This scenario is particularly relevant for antibacterial and anticancer agents (Fig. 1B, C).

This should not be surprising. Since ancient times, humanity has made use of medicinal plants to heal itself, and even today, traditional medicine represents the dominant health care system in many parts of the world and for billions of people (2). This is the case of herbal medicines, the cornerstone of phytotherapy, which include, according to the World Health Organization (WHO), 'herbs, herbal materials, herbal preparations and finished herbal products that contain, as active ingredients, parts of plants, other plant materials or combinations thereof' (3). Several famous examples could be cited, from aspirin to many anticancer drugs (Tab. I).

However, natural product research still suffers from some important limitations. First, the validation of traditional uses. Despite hundreds (or even thousands) of preclinical (in vitro/in vivo) studies, evidence in humans is still scanty, due to the paucity of clinical trials evaluating the real efficacy of natural products. Second, the poor oral bioavailability of natural products. Phytochemicals are xenobiotics metabolized, detoxified and eliminated by phase I and II metabolizing enzymes and phase III transporters involved in efflux mechanisms. This drawback can be bypassed by proper (nano) formulation. Third, natural does not always mean safe. The safety of natural products is rarely investigated and the available information is scanty, as are the phytochemical-drug interactions with possible changes in therapeutic efficacy for some drugs with a narrow therapeutic index (4). These issues call for an evidence-based approach to be followed even for phytotherapeutics, where randomized controlled trials are at the top of the evidence-based pyramid (5).

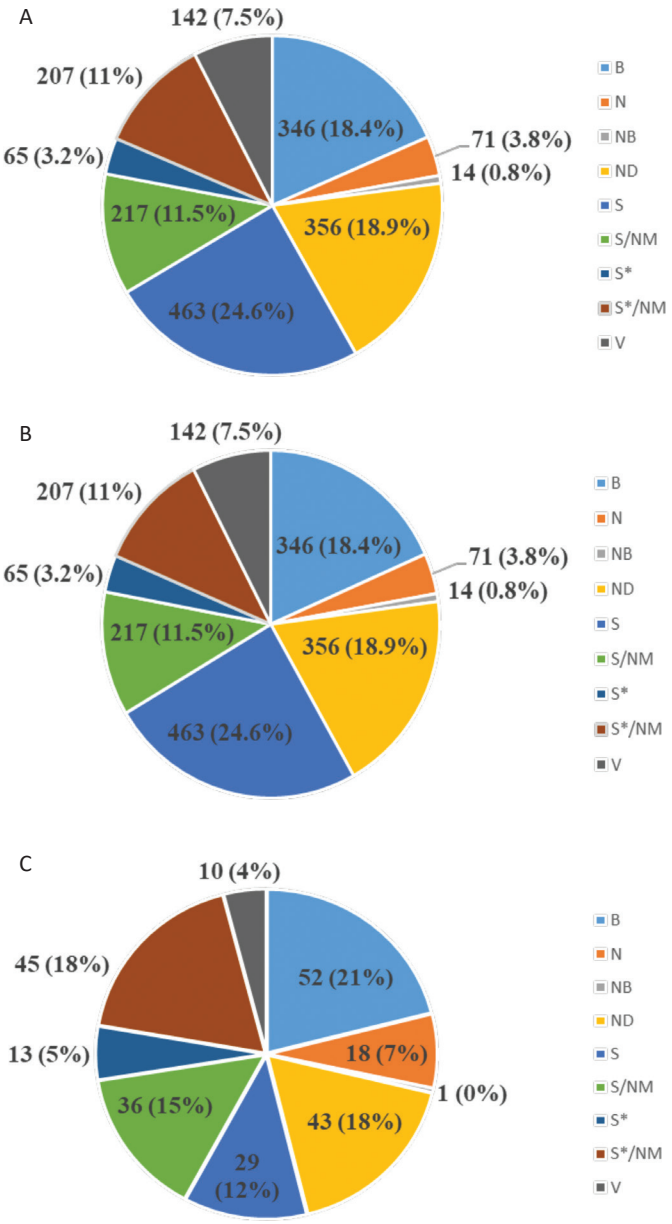
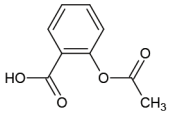
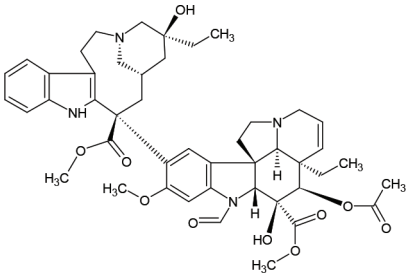
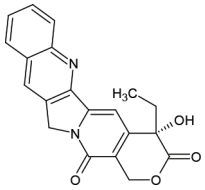
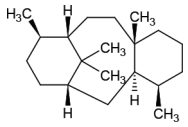
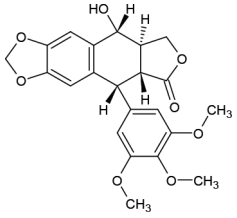
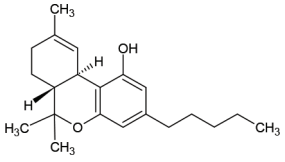
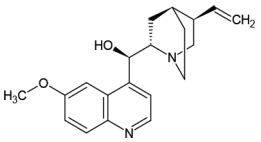
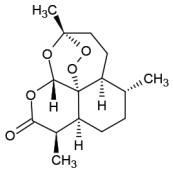


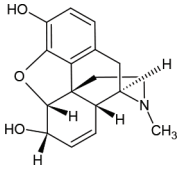
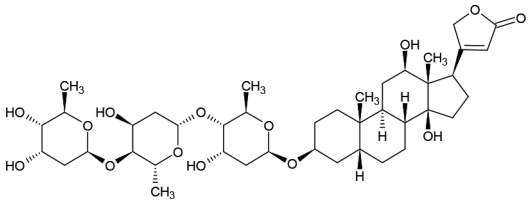
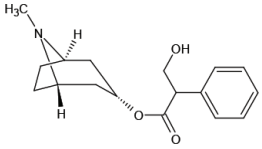
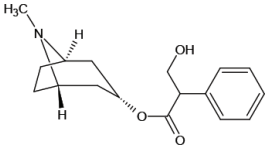
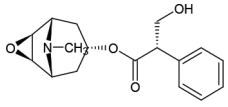
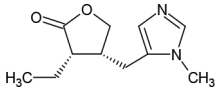
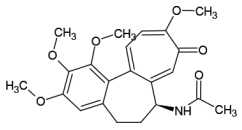
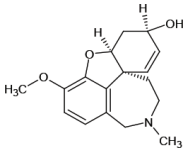
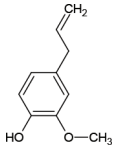
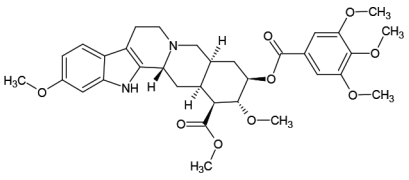
Fig. 1 - A) All new approved drugs by source from 1981 to 2019 (N = 1881). B) All antibacterial drugs by source from 1981 to 2019 (N = 162). C) All anticancer drugs by source from 1981 to 2019 (N = 247). *Categories of sources: B = biological; N = natural product; NB = natural product – botanical; ND = natural product derivative; S = synthetic; S* = synthetic (with pharmacophore from a natural product); V = vaccine. Subcategory: NM = natural product mimic. Adapted from Newman and Cragg (1).*

Received: December 12, 2022
Accepted: December 15, 2022
Published online: January 16, 2023

Corresponding author:
Marcello Iriti
Department of Biomedical, Surgical and Dental Sciences
Università degli Studi di Milano
Milan - Italy
Marcello.iriti@polimi.it

TABLE I - Selected examples of drugs developed from medicinal plants

Medicinal plant	Drugs	Indications	Chemical structure
Salix spp.	Acetylsalicylic acid	Anti-inflammatory, antiaggregant	
Catharanthus roseus	Vinca alkaloids (vincristine, vinblastine, vinorelbine)	Anticancer	
Camptotheca acuminata	Camptothecin derivatives (topotecan, irinotecan)	Anticancer	
Taxus brevifolia	Taxane derivatives (paclitaxel, docetaxel, cabazitaxel)	Anticancer	
Podophyllum peltatum	Podophyllotoxin derivatives (etoposide, teniposide)	Anticancer	
Cannabis sativa	Cannabinoids (tetrahydrocannabinol, cannabidiol)	Psychotropic	
Cinchona spp.	Quinine	Antimalarial	
Artemisia annua	Artemisinin	Antimalarial	

Medicinal plant	Drugs	Indications	Chemical structure
Papaver somniferum	Morphine, codeine	Analgesic	
Digitalis spp.	Glicosidi digitalici (digoxin, digitoxin)	Cardiotonic	
Atropa belladonna	Atropine	Anticholinergic	
Hyoscyamus niger	Hyoscyamine	Anticholinergic	
Datura stramonium	Scopolamine	Anticholinergic	
Pilocarpus jaborandi	Pilocarpine	Cholinergic	
Colchicum autumnale	Colchicine	Antigout	
Galanthus spp.	Galantamine	Cholinesterase inhibitor	
Syzygium aromaticum	Eugenol	Antiseptic, anesthetic	
Rauwolfia serpentina	Reserpine	Antihypertensive	

Not least, the combination of natural products with conventional drugs offers another area of application that should be pursued extensively. This has previously been investigated with natural products used in combination with anticancer drugs and antimicrobials. This therapeutic approach was able to (chemo)sensitize chemoresistant cancer cells, fungi and bacterial strains by inhibiting the cellular active efflux system, a conserved drug resistance mechanism that pumps xenobiotics out of the cell. The rationale for the use of natural products is based on their multitarget action mechanism of particular interest in the treatment of disorders with multistage pathogenesis. In this complex scenario, natural products still offer the best options for finding new active agents/templates and provide the unlimited potential for discovering new structures that can lead to effective drugs in a variety of communicable and non-communicable diseases.

References

1. Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. J Nat Prod. 2020;83(3):770-803. CrossRef PubMed
2. Iriti M. Journal of Phytomoleculs & Pharmacology: 'Why a new journal?' J Phytomol Pharmacol. 2022;1(1):1-2. Online
3. WHO Global Report on Traditional and Complementary Medicine 2019. World Health Organization; 2019. Online Accessed December 2022.
4. Peluso I. Phytomolecules-drug interactions: clinical and nutritional implications. J Phytomol Pharmacol. 2022;1(2):56-57. CrossRef
5. Varoni EM, Lodi G, Iriti M. Efficacy behind activity – phytotherapeutics are not different from pharmaceuticals. Pharm Biol. 2015;53(3):404-406. CrossRef PubMed