Revista Virtual de Química
ISSN 1984-6835

Artigo

Pesquisa com Química e Farmacologia de Produtos Naturais no Brasil: Uma Comparação com 70 Países Selecionados de 5 Continentes

Alves, L. F;* Pontes, T. V. C.

Rev. Virtual Quim., **2017**, *9* (4), 1394-1433. Data de publicação na Web: 27 de junho de 2017

http://rvq.sbq.org.br

Research with Chemistry and Pharmacology of Natural Products in Brazil: A Comparison with 70 Selected Countries from 5 Continents

Abstract: Living organisms (bacteria, fungi, lichens, algae, worms, mushrooms, higher plants, and aquatic and terrestrial animals) produce a plethora of chemical compounds, the 'natural products', that lie at the heart of an ecological interaction, acting as molecular messengers in defense, attack, sexual attraction, territorial and trail marking, in pollination, as venoms, etc. Eventually, human beings make use of them for their own purposes as food additives, flavoring, cosmetics, fragrances, hallucinogens, in pest control, and as therapeutic agents. The present review compares the participation of Brazilian scientists in the chemistry and pharmacology of natural products with that of other scientists from 69 countries in five continents in 36 selected journals. It also shows the analogy between the Human Development Index (HDI) and the rank of the countries with the number published articles. The search was performed in the Web of Knowledge by cross-selecting the names of each journal with that of each country for the period 1945-2013.

Keywords: Brazil; chemistry of natural products; pharmacology of natural products; peer journals.

Resumo

Organismos vivos (bactérias, fungos, liquens, vermes, cogumelos, vegetais superiores, e animais aquáticos e terrestres) produzem uma pletora de substâncias químicas, os 'produtos naturais', que estão no coração de uma interação ecológica, atuando como mensageiros moleculares na defesa, ataque, atração sexual, marcação territorial e de trilha, na polinização, como venenos, etc. Eventualmente, os seres humanos fazem uso deles para o seu próprio benefício como aditivos, flavorizantes, cosméticos, fragrância, alucinógenos, no controle de pestes, e como agentes terapêuticos. Esta revisão compara a participação de cientistas brasileiros na química e farmacologia de produtos naturais com a de cientistas de 69 países de cinco continentes em 36 periódicos selecionados. Ela também mostra a analogia entre o Índice de Desenvolvimento Humano (IDH) e a classificação dos países com o número de artigos publicados. A pesquisa foi realizada na Web of Knowledge através de seleção cruzada do nome de cada periódico com o de cada país no período 1945-2013.

Palavras-chave: Brasil; química de produtos naturais; farmacologia de produtos naturais; periódicos.

* Oswaldo Cruz Foundation, Institute of Pharmaceutical Technology, Department of Natural Products, Rua Sizenando Nabuco 100, Zip Code 21041-050, Manguinhos, Rio de Janeiro-RJ, Brazil.
lucioalves@far.fiocruz.br
DOI: 10.21577/1984-6835.20170082

Volume 9, Número 4 Julho-Agosto 2017

Revista Virtual de Química
ISSN 1984-6835

Pesquisa com Química e Farmacologia de Produtos Naturais no Brasil: Uma Comparação com 70 Países Selecionados de 5 Continentes

Lucio F. Alves,[a,]* Tatiana V. C. Pontes[b]

[a] Oswaldo Cruz Foundation, Institute of Pharmaceutical Technology, Department of Natural Products, Rua Sizenando Nabuco 100, Zip Code 21041-050, Manguinhos, Rio de Janeiro-RJ, Brazil.

[b] Oswaldo Cruz Foundation, Institute of Pharmaceutical Technology, Núcleo de Gestão em Biodiversidade e Saúde. Av. Comandante Guaranys, 447, Zip Code 22775-903, Jacarepaguá, Rio de Janeiro-RJ, Brazil.

* lucioalves@far.fiocruz.br

Recebido em 14 de julho de 2016. Aceito para publicação em 14 de junho de 2017

1. Introduction

According to Edward Wilson our planet harbors approximately 750,000 classified species of insects, 41,000 vertebrates, and 250,000 vascular plants and bryophytes. There remains a complex array of invertebrates, fungi, algae and microorganisms.[1] He also stressed that no one knows the number of these species, nor even to an order of magnitude, but based on his own experience, he suggests that the absolute number falls somewhere between 5 and 30 million. Whatever the true number more than a half are concentrated in 15 countries with megabiodiversity: Australia, Brazil, China, Colombia, Congo, Costa Rica, Ecuador, India, Indonesia, Madagascar, Malaysia, México, Panama, Peru and Zaire (now Democratic Republic of Congo).

It is an obvious truism to say that Earth's resources are limited and that they are continuously being depleted. But why should we be concerned at the disappearance of our biodiversity and why should we explore it from a scientific point of view? Apart from the esthetic reason, two other reasons should be considered. The first is that plants, animals and microorganisms produce thousands of chemical compounds, the 'natural products' that lie at the heart of

an ecological interaction, acting as molecular messengers which play a fundamental role in their everyday life. The second is that human beings make use of them for their own purposes as food additives, flavoring, cosmetics, fragrances, hallucinogens, in pest control, and as therapeutic agents. These reasons are two broad fields of scientific investigation, involves chemical ecology and the pharmacology of natural products

The aim of this review is to analyze the contribution of Brazilian scientists in these fields as registered in 36 selected peer journals in comparison with 69 (70 in total) other countries from five continents.

2. Chemical ecology

The role of these secondary metabolites was unknown until 1959 when Gottfried Fraenkel[2] established that, in plants, some act as defensive mechanisms against insect predation. At the same time, insects also express chemical factors to overcome such defenses in a Darwinian arms race between species. Also in 1959, Karlson and Butenandt[3] proposed the term pheromone, to 'designate substances that are secreted by an animal to the outside and cause a specific reaction in a receiving individual of the same species'.

Some years later, Law and Regnier[4] discussed the production, transmission and perception of pheromones among insects end proposed the name semiochemicals (from the Greek *semion,* a mark or signal) to designate chemical communication between animals and divided them into two broader classes: allomones and kairomones. The first affords adaptive advantage to the producing organisms, the latter to the receiving organisms.

Whittaker and Feeny[5] expanded the discussion to include attack, defense, alarm, aggregation, mate location, warming, recruitment, sexual attraction, mating choice, prey location, territorial and trail marking in animals. In social insects they also act in class recognition. They can also play a part in the competition between plants for water or light, a phenomenon known as allelopathy.

In 1970, in a now classical book, Sondheimer and Simeone[6] penned 'Great rivers that had independent courses for eons have been known to send out branches, which, when they touched formed a mighty new stream. This may also happen on occasion in the sciences. Recently, spectacularly successful methods have been developed for the purification and characterization of natural products in microquantities. At the same time, interest in solving some difficult ecological problems has quickened, due no doubt to social pressures. The result of this has been the development of the new discipline: chemical ecology'.

Indeed, the development of organic and analytic chemistry and molecular pharmacology has reached a point hard to imagine forty years ago and by the understanding of this chemical language, may offer us a better knowledge of how Nature works.[7-9]

Karlson and Butenendt's[3] and Law and Rengier's[4] article were limited to pheromones. However, today it is also well established that pheromones and other semiochemicals (or small molecules, as Meinwald[7] called them) are found in microorganisms[10-16], amphibinas[17-21], spiders[22-28], birds[29-33], marine organisms[34-41], non-human mammals[42-46], and humans.[47-53]

According to Verpoorte[54] there are some 250,000 of such 'natural products' and some 4,000 new ones are reported every year, while Pierre Escoubas, a French researcher who started Venomic Tech, a company that aims to produce drugs form venoms, observed that the number of venomous animals is estimated to be more than 170,000. If, as he says, the average venom contains 250 peptides, a very conservative estimate, this could represent more than a million compounds worthy of investigation.[55] Spider venoms alone are conservatively predicted to contain more than 10 million bioactive principles.[56]

Over 800 different lipophilic alkaloids

have been isolated from six unrelated frog families from five continents. Most of them are sequestered unchanged into the animals' glandular skin.[57] The potential use of such substances as therapeutic drugs has not yet been elucidated. Citron[15] identified 254 volatile compounds of various classes (hydrocarbons, aldehydes, ketones, carboxylic acid and esters, aromatic, and nitrogen compounds) from 50 bacterial strains, several of which act as insect pheromones.

3. Pharmacology of natural products

Although not mentioned by Sondheimer and Simeone's book[6], the use of plants as therapeutic agents can be found in all cultures and is the most ancient source of medicines. Archeological and historical evidences show that herbal medicines were used by our ancestors since the Neolithic Period (about 10,000-12,000 years ago). The Egyptian Papyrus Ebers (c. 1600 BC), clay cuneiforms Tablets from the Ashurbanibal library (c. 650 BC), physicians like Hippocrates (460-377 BC), Galeno (129-199 DC), Avicenna (980-1037 DC) and Paracelsus (1493-1541 DC), to name a few, described the therapeutic properties of medicinal herbs in their works.[58-66] In some cases, evidences have been based on chemical analyses (Gas chromatography-mass spectroscopy, X-ray spectroscopy, Fourier transform infrared spectroscopy and X-ray powder diffraction) as on Tablets discovered onboard the Pozzino shipwreck (second century BC)[67] and on residues of four medicinal tubes dating form Pliny's era in the collection of the British Museum.[68]

However, the use of natural products as therapeutic agents seems to be much older. For example, recent evidences suggest that the Neanderthals (30,000-24,000 years ago) had already a sophisticated knowledge of their surroundings, which included the selection and use of medicinal plants.[69] The use of turtle shell fossils as a therapeutic agent has also been reported.[70]

Natural products are still central in drug discovery, even in the XXI century, with the development of high-throughput screening and combinatory chemistry and motivate chemists, pharmacologists and biologists to examine traditional medicine and herbal pharmacopoeias.[71-95] Although still overlooked, the importance of carnivorous plants[96] and orchids[97] has also captured the interest of researchers in some countries as sources of new phytochemical agents with therapeutic activities.

However, the use of natural products as therapeutic agents is not restricted to higher plants. Chemical substances with pharmacological properties have been isolated from marine organisms (algae, phytoplankton, sponges, cnidarians, bryozoans, mollusks, echinoderms, shrimps, sea cucumbers and fishes),[34-36,38,39,98-122] oils from fish, snake and dolphins,[123] leeches,[124-126] mushrooms,[127-131] endophytic fungi.[132-136]

In his speech 'One man's poison, another man's medicine?', presented in 1990, Professor Norman Bisset[137] mentioned Paracelsus' dictum (penned almost five centuries before) which says: 'What is there that is not poison, all things are poison and nothing [is] without poison. Solely the dose determines that a thing is not a poison'. Since then, Paracelsus' dictum has been scientifically appreciated[138-143] and many highly toxic and venomous substances with therapeutic activities have been isolated from insects (bees, wasps, ants, caterpillars),[144-147] scorpions,[126,148-151] snakes,[152-155] amphibians[156-158] and spiders.[126,143,150,151,159] Spider's silk[160-163] and hemocytes[164] have also been reported as therapeutic agents. Other creatures include snails,[126,165] ticks,[126] centipedes.[126] Even deer velvet extract,[166-170] crocodile oil[171,172], hemoglobin,[173] bile,[174-176] plasma[177] and tissue[178] have also been reported for medicinal uses.

It should also be noted that the use of medicinal plants is not restricted to humans. For example, evidences suggest that European starlings (*Sturnus vulgarias*) bring fresh vegeTable material such as wild carrot (*Daucus carota*), yarrow (*Achillea millefolium*), agrimony (*Agrimonia parviflora*), elm-leaved and rough golden rod (*Solidago spp.*), and fleabane (*Erigeron spp*) for nest building. These plants contain chemical substances that may act to reduce pathogens and ectoparasites.[179] Moreover, farm animals are able to detect the presence of internal parasites or their associated symptoms and modify their diet by the ingestion of medicinal plants with antiparasitic properties.[180] When feeding on plants with a high tannin concentration such as Sulla (*Hedysarum corarium*), sainfoin (*Onobrychis viciifolia*), heather (*Calluna vulgaris*), mastic (*Pistacia lentiscus*), these animals have lower helminth eggloads than those feeding on other plants of similar quality, or the same rations without tannins.[181] But, among animals, self-medication has been more frequently registered in non-human primates such as bonobos (*Pan panicus*), chimpanzees (*Pan troglodytes*), gorillas (*Gorilla gorilla*), lemurs, tamarins, howler monkeys (*Alouatta guariba*) and orangutans (*Pongo abelii*). They make use of medicinal plants to heal wounds and to expel parasites.[182-191]

Scientists are now interested not only in the isolation and identification of these natural products, but also in deciphering how living organisms detect them, how (or why) they perceive them to act as they do and the synergy and mechanisms of action of the active principles responsible for their biological (and sometimes therapeutic) activities.

These data, covering, with few exceptions, reviews published in the period 2012-2013, show that the chemistry and pharmacology of natural products are complex field that have become multidisciplinary. Only an interdisciplinary effort between scientists of several areas (chemistry, pharmacology, botany, zoology, microbiology, agronomy to name a few) are able to produce answers to these questions.

Brazil has three reasons to make a rational use of its natural resources: the first is its own history. Its name derives from 'brazilin', a red natural dye obtained from the wood of the Leguminosae species *Caesalpinia echinata,* called 'pau-brasil', a tree found to be abundant in the new colony and whose pigment was highly appreciated by the upper classes during the 1500 and 1600s. Brazil has also a long tradition in the study of its biodiversity, although during three centuries, from the first colonizers in 1500 to the arrival in Brazil of the Portuguese Royal family in 1808, description, except for the brief period during Dutch and French occupation of small parts of the territory, was almost limited to the Portuguese colonizers themselves.[58,62,63,192-198]

The second reason is its huge biodiversity and the third is the technical and scientific capacity of the research community, I have discussed the first two elsewhere.[58,62,63]

Across the country there are several research centers involved *in the study of medicinal plants (566 groups), ethnopharmacology* (75 groups), marine organisms (49 groups), toxinology and animal venoms (28 groups), allelopathy (63 groups), pheromones (18 groups), chemical ecology (209 groups), chemistry of natural products (409 groups) pharmacology of natural products (148 groups), pharmacognosy (50 groups), phytochemistry (228 groups) and propolis (68 groups).[199]

Several peer journals dedicated specifically to these areas have been created in the last few decades in which scientists have published their results. The aim of this review is to analyze the contribution of Brazilian scientists in these fields as registered in 36 selected of these peer journals in comparison with 69 (70 in total) other countries from five continents.

4. Discussion

In 2005, when invited to write a short article to discuss his own ideas regarding the development of ethnopharmacology in Latin America, Professor João Batista Calixto[200], from the Department of Pharmacology of the Federal University of Santa Catarina, expressed two feelings, the first was the relevance of the topic, and the second the fact, as he perceived it, that the literature on the subject was not very abundant. Analyzing the publication from 9 Latin American countries (Brazil, Mexico, Argentina, Chile, Venezuela, Colombia, Peru, Cuba and Uruguay) in 4 scientific journals (*Phytochemistry, Journal of Ethnopharmacology, Journal of Natural Products* and *Planta Medica*), covering the period 1984-2004, he showed that the total number of articles published by Brazil (853), in these journals, was almost the double of those published by Mexico (448), the second in rank.

Analyses of ethnobiological research in Latin America showed similar results.[201] From 679 articles published in this area, between 1963 and 2012, 289 (41%) were conduct in Brazil and 153 (225) in Mexico.

Here I will extend and update (from the first issue of each journal available on the web to December 2013) these data comparing papers from Brazil in 36 peer journals dedicated to the area of medicinal plants and chemistry of natural products (Table 1), with 69 selected countries from North America (3 countries), Central and South America (13 countries), Europe (26 countries), Asia and Oceania (16 countries) and Africa 14 countries) and those with a big biodiversity (15 countries, distributed, with the exception of Australia, in Latin America, Asia and Africa) (Table 2). Countries were selected based on the following criteria:

1) Developed countries (or from the First World)

2) Countries from East Europe

3) Developing countries (or from the Third World)

4) Countries with a 'big biodiversity' (in italic on the Table. With the exception of Australia, the countries in criteria 3 and 4 overlap).

It should to be noted that *Lloydia* and *Natural Product Letters* are the former names of *Journal of Natural Product* and *Natural Product Research,* respectively. The average of Brazil is 4.73%.

Table 3 shows total numbers of articles published by the selected countries in the selected peer journals.

Table 1 Participation of Brazil in the 36 selected peer journals

TITLE	Abbreviation	Impact Factor	1st volume	Available at web since the journal was indexed at Web of Knowledge	Number of articles published by Brazil	N^0 of article available	%
1. Biochemical Systematics & Ecology	BSE	1.153	1973	Vol. 5, 1977	335	4.184	6.60
2. BMC Complementary and Alternative Medicine	BMC	2.08	2001	Vol. 8, 2008	49	978	4.33
3. Chemical Senses	CSS	3.22	1976	Vol. 5, 1980	10	7.032	0.01
4. Chemico-Biological Interactions	CBI	2.967	1969	Vol. 3, 1971	136	6.043	2.32
5. Chemistry and Biodiversity	CBD	1.808	2004	Vol. 1, 2004	62	1.863	3.32
6. Chemistry of Natural Compounds	CNC	0.599	1965	Vol. 35, 1999	31	3.327	0.93
7. Chemoecology	CHE	1.945	1990	Vol. 7, 1996	16	489	0.20
8. Evidence Based Complementary Alternative Medicine	EBCAM	1.772	2004	Vol. 1, 2004	173	3.260	5.30
9. Fitoterapia	FIT	2.139	1900	Vol. 69, 1969	158	2.586	6.10
10. Flavour and Fragrance journal	FFJ	1.824	1985	Vol. 7, 1992	72	1.539	4.67

11. Food Chemistry	**FCH**	**4.072**	**1976**	**Vol. 2, 1977**	**527**	**14.946**	**3.52**
12. Journal of Agricultural and Food Chemistry	JAFC	2.906	1953	Vol. 1, 1953	539	36.692	1.46
13. Journal of Alternative and Complementary Medicine	JACM	1.464	1994	Vol. 4, 1998	23	2.455	0.93
14. Journal of Chemical Ecology	JCE	2.462	1975	Vol. 3, 1977	120	6.141	1.95
15. Journal of Essential Oil Research	JEOR	0.553	1989	Vol. 12, 2000	237	2.151	11.0
16. Journal of Ethnobiology and Ethnomedicine	JEE	2.42	2005	Vol, 5, 2009	39	252	15.47
17. Journal of Ethnopharmacology	JEP	2.775	1979	Vol. 1, 1979	647	8020	8.06
18. Journal of Medicinal Food	JMF	1.642	1998	Vol. 7, 2004	119	1.447	8.22
19. Journal of Natural Products	JNP	3.285	1979	Vol. 24, 1961	241	10.991	2.19
20. Lloydia	LLO	-	1937	Vol. 42, 1979	6	788	0.76
21. Marine Drugs	MAR	3.978	2003	Vol. 3, 2005	39	968	4.02
22. Molecules	MOL	2.428	1996	Vol. 2, 1997	282	5.564	4.97
23. Natural Product Communications	NPC	0.956	2006	Vol. 1, 2006	148	2.794	5.29
24. Natural Product Letters	NPL	-	1991	Vol. 6, 1995	21	564	3.72
25. Natural Product Reports	NPREP	10.178	1981	Vol. 1, 1981	14	1.288	1.08

26. Natural Product Research	NPRES	1.031	1996	Vol. 7, 2003	121	2.402	5.03
27. Peptides	PEP	2.522	1980	Vol. 1, 1980	215	8.264	2.60
28. Pharmaceutical Biology	PHB	1.206	1961	Vol. 36, 1998	164	2.861	5.73
29. Phytochemical Analysis	PAN	2.48	1990	Vol. 2, 1991	86	1.340	6.41
30. Phytochemistry	PTC	3.575	1961	Vol. 1, 19610	876	29.358	2.98
31. Phytochemistry Letters	PTL	1.353	2008	Vol. 1, 2008	27	581	4.64
32. Phytochemistry Review	PCR	4.15	2002	Vol. 8, 2009	8	202	3.96
33. Phytomedicine	PTM	3.258	1995	Vol. 2, 1995	195	2.414	8.07
34. Phytotherapy Research	PTR	2.068	1987	Vol. 3, 1989	259	4.750	5.45
35. Planta Medica	PLM	2.348	1952	Vol. 23 1965	609	16.281	3.74
36. Toxicon	TOX	2.792	1963	Vol. 4, 1966	1134	8.674	13.07

Table 2. Participation of 70 countries in 36 selected peer Journals

Country	BMC	BSE	CBD	CBI	CHE	CNC	CSS	EBCAM	FCH	FIT	FFJ	JAC M	JAFC	JCE	JEOR	JEE	JEP	JMF	Total
1. Algeria	1	25	4	2	0	69	0	0	20	8	20	2	16	1	45	1	13	6	233
2. Argentina	1	111	21	27	10	1	10	14	120	36	20	1	233	25	45	4	136	11	826
3. Australia	48	123	24	126	10	1	133	85	343	25	20	114	607	238	45	5	94	6	2047
4. Austria	5	54	41	22	3	9	26	52	86	12	45	14	162	14	27	5	54	1	632
5. Belgium	3	64	46	47	16	6	15	6	255	13	16	4	499	71	14	5	116	0	1196
6. Botswana	1	6	1	0	0	0	0	2	8	3	0	0	3	1	0	0	6	3	34
7. Brazil	***49***	335	62	136	10	31	10	173	527	158	72	23	539	120	237	39	647	119	3287
8. Bulgaria	0	30	5	12	3	6	0	6	29	22	5	0	27	14	17	1	22	1	200
9. Cameroon	41	29	5	0	0	5	0	9	18	35	18	0	8	1	12	5	104	2	292
10. Canada	34	174	20	214	37	19	118	67	517	16	10	87	1804	515	29	14	133	40	3848
11. Chile	0	49	1	21	9	1	9	5	72	15	1	0	96	40	5	1	54	3	382
12. China	127	561	419	249	12	625	33	1106	1774	655	46	196	2356	136	29	9	1333	78	9744
13. Colombia	3	22	3	2	0	4	0	2	19	10	4	3	54	13	26	3	29	0	197
14. Congo	0	*2*	0	0	0	0	0	0	1	5	1	0	0	1	5	1	11	0	27
15. Costa Rica	*0*	8	1	0	1	0	1	0	2	2	2	0	12	14	11	0	15	0	69
16. Cuba	2	3	3	3	0	0	0	0	19	9	11	3	36	3	116	1	20	17	246
17. Denmark	6	80	11	18	6	1	22	10	166	5	22	15	457	33	8	6	61	3	930
18. *Ecuador*	0	1		0	0	0	0	0	12	2	2	0	13	1	3	2	10	0	46

19.	**Egypt**	4	64	7	7	1	24	4	11	270	44	9	4	72	16	15	1	38	17	608
20.	**England**	41	231	50	546	23	22	260	70	834	41	43	285	876	372	28	6	240	13	3981
21.	**Finland**	1	17	18	85	23	1	10	3	92	4	11	3	344	83	6	3	13	2	719
22.	**France**	9	389	90	282	46	71	494	29	631	78	196	11	1163	256	184	1	257	20	4207
23.	**Germany**	48	228	156	241	120	31	558	155	398	65	109	99	1491	393	39	13	19	506	4669
24.	**Greece**	2	57	14	15	3	10	1	1	315	7	51	7	281	21	66	0	18	20	889
25.	***Guatemala***	*0*	1	0	0	0	0	0	3	3	1	2	0	14	0	2	0	23	0	49
26.	**Hungary**	0	16	19	25	6	0	8	5	39	14	4	3	107	35	10	2	10	5	308
27.	**India**	65	*85*	99	305	6	75	5	179	741	402	126	92	661	69	197	13	1078	125	4323
28.	***Indonesia***	1	*5*	5	1	2	1	0	4	21	18	1	1	33	6	1	1	15	1	117
29.	**Iran**	5	38	18	12	1	115	2	25	185	40	107	31	51	4	281	0	98	20	1033
30.	**Ireland**	3	3	6	7	0	0	2	1	178	2	5	2	182	4	0	0	12	4	411
31.	**Israel**	9	24	10	49	15	2	51	37	55	5	9	51	330	103	0	0	48	12	810
32.	**Italy**	13	191	158	292	14	35	164	79	962	201	150	43	1756	99	140	18	232	45	4592
33.	**Japan**	27	244	155	295	35	28	1473	231	603	85	81	60	2327	361	42	2	326	62	6437
34.	**Kenya**	2	16	0	4	4	1	0	0	37	14	8	0	18	51	6	5	53	0	219
35.	**Korea**	82	41	22	116	1	49	26	385	464	78	15	98	767	45	8	1	649	398	3245
36.	***Madagascar***	0	7	8	0	0	0	0	0	2	5	1	0	1	1	11	1	6	0	43
37.	**Malaysia**	80	*25*	8	6	5	6	1	145	301	29	18	8	66	26	29	2	114	13	882
38.	**Mexico**	9	59	8	24	5	5	23	21	159	41	7	5	270	60	14	21	248	17	996
39.	**Northern Ireland**	0	5	0	2	0	6	5	0	27	1	0	5	40	0	0	0	1	0	92

40.	**New Zealand**	**5**	**59**	**4**	**40**	**5**	**0**	**23**	**3**	**172**	**3**	**3**	**7**	**300**	**115**	**5**	**1**	**8**	**8**	**761**
41.	**Netherlands**	4	47	24	203	20	3	165	7	189	10	32	25	555	178	19	11	93	1	1586
42.	**Nigeria**	22	4	21	7	0	2	7	11	331	71	24	7	58	6	41	3	271	57	943
43.	**Norway**	14	50	6	36	4	3	67	8	144	2	4	36	182	29	5	3	32	2	627
44.	**Pakistan**	37	8	34	4	0	31	1	15	78	51	4	3	34	4	2	8	100	5	419
45.	***Panama***	*0*	5	0	0	0	0	0	0	2	3	2	0	11	14	3	0	18	0	58
46.	**Paraguay**	0	0	1	5	0	0	0	0	0	6	0	0	2	1	3	0	26	1	45
47.	***Peru***	*0*	3	1	0	0	0	0	3	23	3	7	0	19	1	2	3	38	2	105
48.	**Poland**	3	67	28	77	3	20	0	31	325	37	35	5	293	39	287	30	10	10	1300
49.	**Portugal**	2	35	7	16	7	2	13	10	351	14	67	3	423	14	32	7	38	9	1050
50.	**Romania**	4	10	5	2	0	14	1	4	31	4	0	1	13	1	2	0	4	6	102
51.	**Russia**	1	26	23	32	1	764	44	5	20	11	2	9	52	13	11	2	4	3	1023
52.	**Saudi Arabia**	21	7	6	7	0	8	0	21	63	11	0	4	13	0	6	0	51	13	231
53.	**Scotland**	1	82	3	67	3	11	8	7	84	20	14	27	164	13	6	2	21	2	535
54.	**South Africa**	32	119	6	16	4	3	7	19	85	13	9	7	141	57	27	8	278	14	845
55.	**Spain**	9	165	56	121	18	12	83	29	1767	46	59	21	3113	132	78	8	195	25	5937
56.	**Sweden**	16	35	8	289	31	1	122	18	160	7	2	19	312	249	2	5	69	3	1348
57.	**Switzerland**	7	18	25	47	28	0	112	22	86	15	54	28	430	111	3	4	91	2	1083
58.	**Taiwan**	36	28	47	107	1	46	9	438	521	16	2	87	1192	42	6	0	251	28	2857
59.	**Tanzania**	3	1	0	1	0	0	2	0	18	3	1	2	4	3	2	7	35	0	82

60.	**Thailand**	25	33	17	15	0	11	1	36	271	60	10	10	121	3	6	2	170	5	796
61.	**Tunisia**	11	25	29	10	1	7	0	5	107	7	12	0	64	0	31	1	11	8	329
62.	**Turkey**	6	68	15	25	0	175	4	15	489	64	62	28	166	4	132	1	173	78	1505
63.	**Uganda**	1	0	0	0	0	0	4	0	7	1	0	4	8	2	0	5	24	1	57
64.	**Uruguay**	0	3	0	0	0	0	0	0	10	1	15	1	29	8	2	0	11	0	80
65.	**USA**	143	649	222	1495	149	26	2328	481	1115	143	75	1106	7824	2598	118	37	508	265	19282
66.	**USSR**	0	4	0	7	0	0	8	0	1	0	0	0	5	4	0	0	4	0	33
67.	**Venezuela**	0	30	3	3	0	3	0	5	22	14	11	0	32	17	8	1	21	4	174
68.	**Wales**	6	50	2	13	0	0	16	11	49	4	25	22	90	42	62	0	14	1	407
69.	**Yugoslavia**	0	19	0	7	0	2	3	0	9	8	17	1	26	0	40	0	1	0	133
70.	***Zaire***	0	*2*	0	0	0	0	1	0	1	2	0	1	1	0	0	0	20	0	28
Total		1131	5075	2111	5845	702	2404	6493	4125	16836	2856	1816	2734	33449	6946	2694	341	8946	2123	106627

Table 2. continued

Country	JNP	LLO	MAR	MOL	NPC	NPL	NPREP	NPRES	PAN	PCR	PEP	PHB	PLM	PTC	PTL	PTM	PTR	TOX	Total
1. Algeria	8	0	1	21	40	0	0	7	4	0	2	10	28	22	3	3	4	13	399
2. Argentina	121	7	4	176	53	12	1	19	13	0	76	38	91	323	7	48	67	88	1970
3. *Australia*	350	0	42	117	70	9	42	42	26	5	172	23	152	717	12	35	76	464	4401
4. Austria	55	1	2	43	73	2	9	9	31	8	54	9	463	151	7	463	39	11	2062
5. Belgium	110	1	8	50	23	5	6	7	32	3	211	8	293	289	13	293	41	54	2643
6. Botswana	4	0	0	0	10	0	1	6	1	0	0	0	15	34	5	1	2	3	116
7. *Brazil*	241	6	39	282	148	21	14	121	86	8	215	164	609	876	27	195	259	1134	7732
8. Bulgaria	23	0	0	19	38	2	0	34	17	0	14	8	78	139	2	78	20	25	697
9. Cameroon	73	0	0	9	40	5	2	22	3	1	0	21	99	152	25	7	23	1	775
10. Canada	303	22	24	81	57	9	25	24	35	7	557	275	168	800	8	34	57	115	6449
11. Chile	95	4	5	59	34	6	1	13	7	4	17	10	64	289	2	11	38	51	1092
12. *China*	1118	0	212	1257	321	25	61	536	196	5	657	262	1391	970	132	379	506	346	18118
13. Colombia	34	0	4	34	17	5	0	8	2	1	24	11	34	69	5	0	7	29	481
14. *Congo*	1	0	0	0	1	0	0	0	0	1	0	1	6	5	0	2	0	0	44
15. *Costa Rica*	26	0	0	1	2	0	0	1	0	0	0	7	19	53	0	0	1	215	394
16. Cuba	9	0	1	13	25	0	0	0	0	0	5	4	25	22	3	6	23	35	417

17.	**Denmark**	85	2	12	20	8	2	1	9	10	4	109	17	118	343	3	118	15	26	1832
18.	***Ecuador***	9	0	0	0	1	0	0	0	0	0	2	2	7	12	0	0	2	2	83
19.	**Egypt**	144	2	15	166	76	7	2	80	12	0	6	58	331	390	21	23	46	73	2060
20.	**England**	215	24	17	73	75	6	361	16	66	8	400	59	506	2216	27	506	211	368	9135
21.	**Finland**	17	0	6	26	10	0	3	0	19	2	35	6	159	83	5	159	10	34	1293
22.	**France**	605	11	55	179	145	42	37	86	79	11	523	48	786	1591	39	786	107	514	9851
23.	**Germany**	506	4	65	178	158	73	83	85	112	30	327	58	1583	1954	48	1583	179	296	11991
24.	**Greece**	60	0	6	46	18	18	2	9	9	0	28	7	329	62	5	329	25	11	1853
25.	***Guatemala***	3	2	0	0	0	0	0	0	0	0	0	5	7	3	0	1	4	3	77
26.	**Hungary**	52	2	4	32	39	7	2	6	5	0	143	3	175	112	1	175	46	14	1126
27.	**India**	351	24	12	80	241	31	16	344	63	17	60	496	779	2075	16	247	679	186	10040
28.	***Indonesia***	85	0	11	10	26	0	0	13	7	3	0	3	39	70	10	4	12	3	413
29.	**Iran**	25	12	1	113	50	1	0	107	7	0	25	94	433	80	7	41	103	33	2165
30.	**Ireland**	13	0	10	23	17	0	17	1	2	1	8	1	32	54	0	32	11	48	681
31.	**Israel**	92	4	5	13	12	1	5	2	7	2	99	5	54	270	4	3	15	209	1612
32.	**Italy**	587	5	63	234	262	31	18	225	77	22	535	46	508	1034	24	508	196	212	9179
33.	**Japan**	1402	10	71	291	221	89	51	110	51	2	850	96	1070	4202	66	197	403	363	15982
34.	**Kenya**	27	4	0	2	12	3	0	2	2	0	0	6	31	98	11	4	11	8	440
35.	**Korea**	335	1	34	197	58	5	6	52	27	2	79	103	820	168	10	72	520	48	5782
36.	***Madagascar***	33	0	0	2	8	0	0	8	1	0	0	1	20	25	0	0	1	3	145

37.	***Malaysia***	79	0	4	256	45	12	2	39	9	3	4	60	120	134	9	21	24	46	1749
38.	***Mexico***	229	6	11	127	54	22	2	33	17	5	72	70	237	380	9	49	72	177	2568
39.	**Northern Ireland**	3	0	0	3	9	0	26	4	0	1	71	3	5	20	1	5	6	12	261
40.	**Netherlands**	153	7	13	23	8	2	12	6	56	16	146	7	269	292	5	269	18	41	2929
41.	**New Zealand**	156	1	9	11	8	2	23	3	10	4	41	3	27	335	2	3	14	63	1476
42.	**Nigeria**	35	6	0	11	36	2	1	16	0	0	0	104	285	97	2	29	156	19	1742
43.	**Norway**	11	4	18	29	7	0	2	4	8	3	15	8	36	131	2	36	11	76	1028
44.	**Pakistan**	150	2	1	53	58	38	7	165	1	1	6	39	136	274	14	13	97	6	1480
45.	***Panama***	50	1	1	3	7	1	0	4	1	0	0	21	35	33	0	1	5	2	223
46.	**Paraguay**	10	0	0	1	0	0	0	1	0	0	4	3	12	10	0	6	10	1	103
47.	***Peru***	21	0	0	1	5	0	0	0	1	0	0	3	22	13	2	5	4	15	197
48.	**Poland**	23	1	6	144	48	2	0	15	31	8	166	12	204	255	11	204	48	29	2507
49.	**Portugal**	36	0	44	80	28	8	8	34	32	5	24	13	225	143	8	225	22	66	2051
50.	**Romania**	0	0	2	55	3	1	0	10	6	0	5	1	100	4	1	2	11	6	309
51.	**Russia**	69	0	18	72	60	1	3	9	6	1	36	1	51	84	3	10	20	56	1523
52.	**Saudi Arabia**	41	0	11	146	21	1	0	29	1	0	1	27	67	81	18	14	58	44	791
53.	**Scotland**	89	3	8	11	19	6	121	8	20	1	30	12	81	544	5	10	27	107	1637
54.	**South Africa**	77	1	6	64	46	2	48	16	13	0	53	57	154	345	15	30	40	69	1881
55.	**Spain**	461	1	55	219	90	32	50	30	77	25	200	34	412	1063	17	38	150	158	9049
56.	**Sweden**	78	5	3	29	9	12	5	3	12	5	264	2	96	243	4	46	32	100	2296

57. Switzerland	165	2	12	85	26	3	18	3	69	2	110	27	507	426	7	75	47	94	2761
58. Taiwan	503	1	78	161	72	1	4	52	18	0	59	50	495	368	10	67	123	273	5192
59. Tanzania	10	1	1	0	8	4	1	8	1	0	0	9	22	21	1	0	6	2	177
60. Thailand	242	0	7	65	52	0	0	49	21	1	8	90	378	265	47	36	58	93	2208
61. Tunisia	12	0	4	12	11	1	0	46	1	0	11	6	20	24	2	5	6	38	528
62. *Turkey*	135	5	3	72	71	14	0	86	7	0	63	151	424	287	15	29	115	21	3003
63. Uganda	2	0	0	1	2	0	0	0	0	0	0	1	4	6	4	0	1	1	79
64. Uruguay	6	1	1	10	8	2	0	3	5	2	6	2	5	16	0	3	5	17	172
65. USA	2572	57	134	429	286	36	222	104	113	19	2529	415	1290	2145	57	187	351	1448	31676
66. USSR	3	0	0	0	0	0	2	0	2	0	2	0	15	28	0	0	1	49	135
67. Venezuela	25	0	1	2	58	3	1	6	5	0	1	8	28	51	0	4	10	78	455
68. Wales	31	3	6	11	12	0	18	0	6	0	26	1	24	371	4	8	14	81	1023
69. Yugoslavia	9	1	0	6	0	0	0	0	0	0	5	7	26	43	0	3	13	58	304
70. *Zaire*	3	0	0	0	1	0	0	0	0	0	0	2	21	11	1	2	0	0	69
	12706	257	1186	6039	3557	625	1342	2790	1558	249	9191	3214	17155	28296	824	7778	5334	8384	110485

Table 3. Total numbers of papers published by country, values of HDI and rank in HDI

Country	Total of papers	percentage	HDI	Rank in HDI
1. USA	31676	14,51	0,937	3^0
2. China	18118	8,34	0,669	101^0
3. Japan	15982	7,36	0,912	10^0
4. Germany	11991	5,52	0,920	5^0
5. India	10040	4,62	0,554	138^0
6. France	9851	4,53	0,893	20^0
7. Italy	9179	4,22	0,881	25^0
8. England	9135	4,20	0,875	26^0
9. Spain	9049	4,16	0,885	23^0
10. Brazil	7732	3,56	0,730	85^0
11. Canada	6449	2,97	0,911	11^0
12. Korea	5782	2,66	0,909	120
13. Taiwan	5192	2,39	-	-
14. Australia	4401	2,02	0,938	2^0
15. Turkey	3003	1,38	0,772	90^0
16. Switzerland	2761	1,27	0,913	9^0
17. Belgium	2643	1,21	0,987	17^0
18. Mexico	2568	1,18	0,775	61^0
19. Poland	2507	1,15	0,831	39^0
20. Netherlands	2301	1,05	0,921	4^0
21. Sweden	2296	1,05	0,918	7^0
22. Thailand	2208	1,01	0,690	103^0
23. Iran	2165	0,99	0,742	76^0
24. New Zealand	2104	0,96	0,919	6^0
25. Austria	2062	0,94	0,985	18^0
26. Egypt	2060	0,94	0,662	112^0
27. Portugal	2051	0,94	0,816	45^0
28. Argentina	1970	0,90	0,811	45^0
29. South Africa	1881	0,86	0,629	121^0
30. Greece	1853	0,85	0,860	29^0
31. Denmark	1832	0,84	0,901	15^0
32. Malaysia	1749	0,80	0,769	64^0
33. Nigeria	1742	0,80	0,471	153^0
34. Scotland	1637	0,75	-	-
35. Israel	1612	0,74	0,900	16^0
36. Russia	1523	0,70	0,788	55^0
37. Pakistan	1480	0,68	0,515	146^0
38. Finland	1293	0,59	0,982	21^0
39. Hungary	1126	0,51	0,831	37^0
40. Chile	1092	0,50	0,819	40^0
41. Norway	1028	0,47	0,955	1^0
42. Wales	1023	0,47	-	-
43. Saudi Arabia	791	0,36	0,786	57^0
44. Cameroon	775	0,35	0,495	150^0
45. Bulgaria	697	0,32	0,782	57^0
46. Ireland	681	0,31	0,916	7^0
47. Tunisia	528	0,24	0,713	93^0

48. Colombia	481	0,22	0,722	91^0
49. Venezuela	455	0,20	0,748	71^0
50. Kenya	440	0,20	0,519	145^0
51. Cuba	417	0,19	0,780	59^0
52. Indonesia	413	0,19	0,629	121^0
53. Algeria	399	0,18	0,712	94^0
54. Costa Rica	394	0,18	0,780	59^0
55. Romania	309	0,14	0,786	56^0
56. Yugoslavia	304	0,14	-	-
57. North Ireland	261	0,12	-	-
58. Panama	223	0,10	0,773	62^0
59. Peru	197	0,09	0,741	77^0
60. Tanzania	177	0,08	0,476	152^0
61. Uruguay	172	0,07	0,792	51^0
62. Madagascar	145	0,06	0,483	151^0
63. USSR	135	0,06	-	-
64. Botswana	116	0,05	0,634	119^0
65. Paraguay	103	0,04	0,669	111^0
66. Ecuador	83	0,03	0,724	89^0
67. Uganda	79	0,03	0,456	160^0
68. Guatemala	77	0,03	0,581	133^0
69. Zaire	69	0,03	0,304	186^0
70. Congo	44	0,02	0,534	142^0

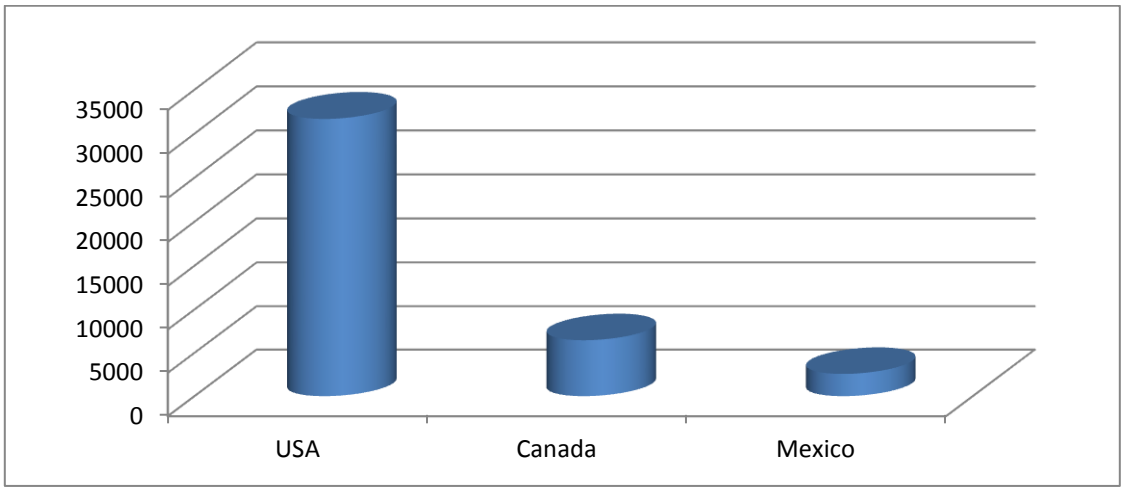
This Table ranks all countries by the increasing number of published papers, its percentage with total of articles published by all counties in all journals, and the values and ranks according to the HDI. These data deserve some comments. The first is that the Unites States alone, with 31,676 articles, is responsible for 14.51% of the total of 217,112 and corresponds to almost the double published by China, the second in the rank, with 18,118 (or 8.34%). This Table also shows that the ten first countries of the rank, seven of which are classified as very highly developed countries, respond for almost 120.000, or more than 50% of the total of papers published, and only three, China, India and Brazil with the second, fifth and tenth position respectively have a megabiodiversity. Brazil is in the best situation when HDI is considered. The country occupies the 85^a position and the India the lowest (138^{th}). China is somewhere between the two (101^{th}). Australia, the second according to the HDI (0.938) and the 14^{th} according to the number of papers published, is the only country with a very high economical level as well as a megabiodiversity.

North America

North America has only three countries, one with a megabiodiversity (Mexico), but the participation of the United States gives a privileged position not only in the region, but also in the world. The country is responsible for more than a quarter (77.84%) of the papers produced there, or about 5 and 10 times more than Canada and Mexico (TableS 4 and 5 and Graphic 1).

Table 4. Number of papers published by North American countries in the selected peer journals, values and ranks of HDI

Country	N° of papers	%	HDI	Rank in HDI
USA	31676	77,84	0.937	3rd
Canada	6449	15,84	0.911	11th
Mexico	2568	6,31	0.775	61st
Total	40693			



Graphic 1. Number of papers published by North American countries in the selected peer journals

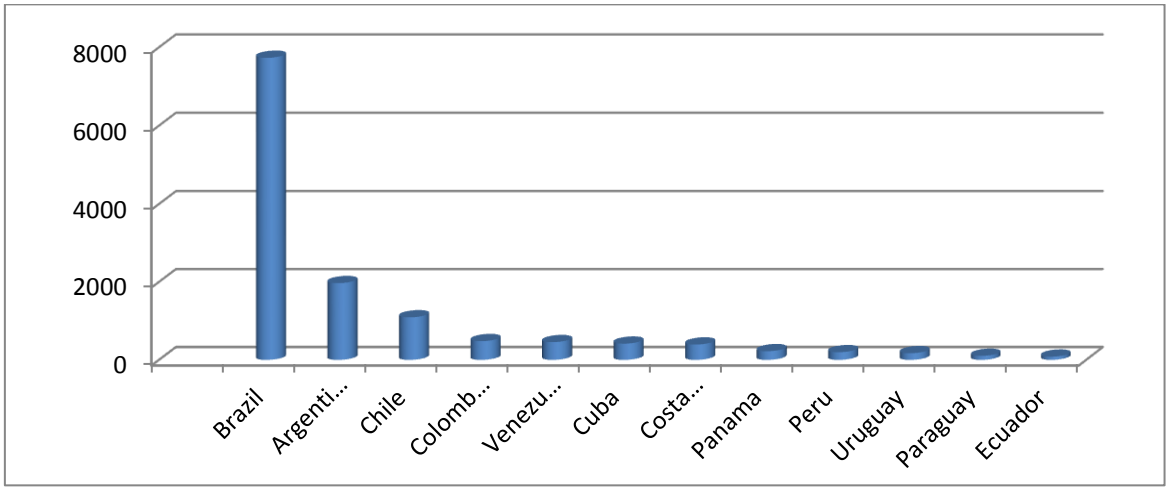
Central and South America

Central and South America and Caribbean (only Cuba), is the geoGraphical region having the greatest number of countries with a megabiodiversity. Six altogether. However, the region produces only 113.396 articles or one fifth of those of Europe and Asia and Oceania and one third of those of North America. Brazil is the leader among these 13 countries, with 7.732 articles, which corresponds to nearly 55% of the articles published in the area and more than three times the total for Argentina, the second country in the rank.

Table 5. Number of papers published by Central, South and Caribbean (Cuba) countries in the selected peer journals, values and ranks of HDI

Country	N0 of papers	%	HDI	Rank
1. Brazil	7732	57,71	0,730	85th
2. Argentina	1970	14,70	0,811	45th
3. Chile	1092	8,15	0.819	40th

4. Colombia	481	3,59	0.772	91st
5. Venezuela	455	3,39	0.748	71st
6. Cuba	417	3,11	0.780	59th
7. Costa Rica	394	2.94	0.780	59th
8. Panama	223	1,66	0.773	62nd
9. Peru	197	1,47	0.741	77th
10. Uruguay	172	1,28	0.792	51st
11. Paraguay	103	0,76	0.669	111st
12. Ecuador	83	0,61	0.724	89th
13. Guatemala	77	09,57	0.581	133rd
Total	13396			



Graphic 2. Number of papers published by Central, South and Caribbean (Cuba) countries in the selected peer journals

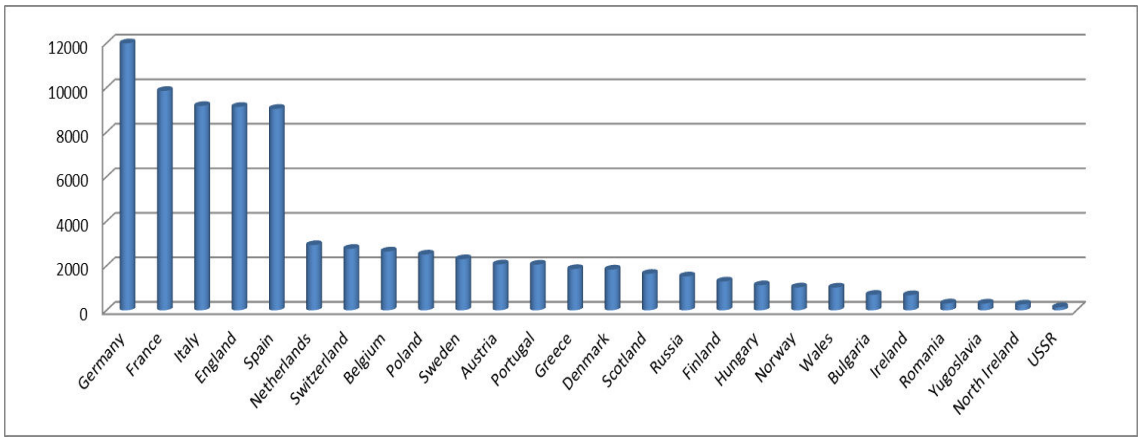
Europe

With 26 countries analyzed, Europe occupies the first rank in terms number of published articles (80.156). Germany, is in the first position in the continent with 11.991 articles (14.95%), followed by France (9.851 articles or 12.28%) and Italy (9.179 papers or 11.45%). (Tables 8 and 9 and Graphic 3).

Table 6. Number of papers published by European countries in the selected peer journals, values and ranks of HDI

Country	N^0 of papers	%	HDI	Rank
1. Germany	11991	14,95	0.920	5th
2. France	9851	12,28	0.893	20th
3. Italy	9179	11,45	0.881	25th

4. England	9135	11,39	0.875	26th
5. Spain	9049	11,28	0.885	23rd
6. Netherlands	2929	3,65	0.921	4th
7. Switzerland	2761	3,44	0.913	9th
8. Belgium	2643	3,29	0.987	17th
9. Poland	2507	3,12	0.831	39th
10. Sweden	2296	2,86	0.918	7th
11. Austria	2062	2,57	0.985	18th
12. Portugal	2051	2,55	0.816	45th
13. Greece	1853	2,31	0.860	29th
14. Denmark	1832	2,28	0.901	15th
15. Scotland	1637	2,04	-	-
16. Russia	1523	1,90	-	-
17. Finland	1293	1,61	0.982	21st
18. Hungary	1126	1,40	0.831	37th
19. Norway	1028	1,28	0.955	1st
20. Wales	1023	1,27	-	-
21. Bulgaria	697	0,86	0.782	57th
22. Ireland	681	0,84	0.916	7th
23. Romania	309	0,38	0.786	56th
24. Yugoslavia	304	0,37	-	-
25. North Ireland	261	0,32	-	-
26. USSR	135	0,16	-	-
Total	80156			



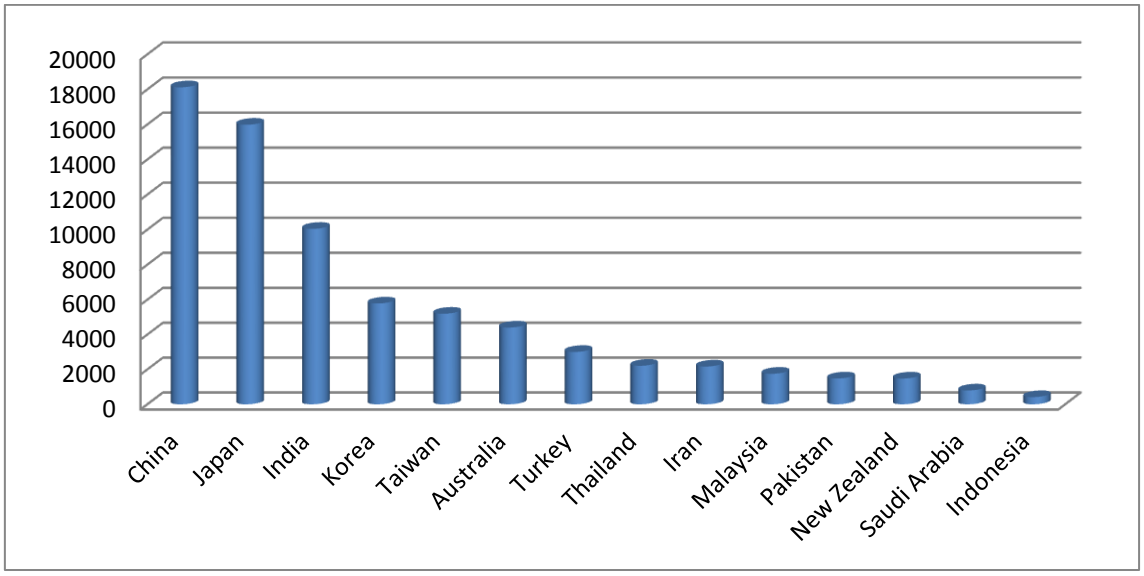
Graphic 3. Number of papers published by European countries in the selected peer journals

Asia and Oceania

After Europe come Asia and Oceania, with 72,800 papers or 33.53% of the world total. The region has 5 countries with a megabiodiversity (Australia, China, India, Indonesia and Malaysia), among a total of 15 analyzed (Tables 10 and, GRAPH 4). With 18,118 pap1ers (24.88%), China predominates in the region. Japan appears very close in the second place (115,982 articles) which corresponds to 21.95%. India, Australia and Malaysia are in the 3rd, 6th and 10th places respectively.

Table 7. Number of papers published by Asian countries, value of HDI and rank

Country	N° of papers	Percentage	Value of HDI	Rank in HDI
1. China	18118	24.88	0.669	101st
2. Japan	15982	21.95	0.918	10th
3. India	10040	13.79	0.554	138th
4. Korea	5782	7,94	0.909	12th
5. Taiwan	5192	7.13	-	-
6. Australia	4401	6.04	0.938	2nd
7. Turkey	3003	4.12	0.772	90th
8. Thailand	2208	3.03	0.690	103rd
9. Iran	2165	2.97	0.742	76th
10. Malaysia	1749	2.40	0.796	64th
11. Pakistan	1480	2.03	0.515	146th
12. New Zealand	1476	2.02	0.919	6th
13. Saudi Arabia	791	1.08	0,786	57th
14. Indonesia	413	0.56	0.629	121st
Total	72800			



Graphic 4. Number of papers published by Asian and Oceania countries

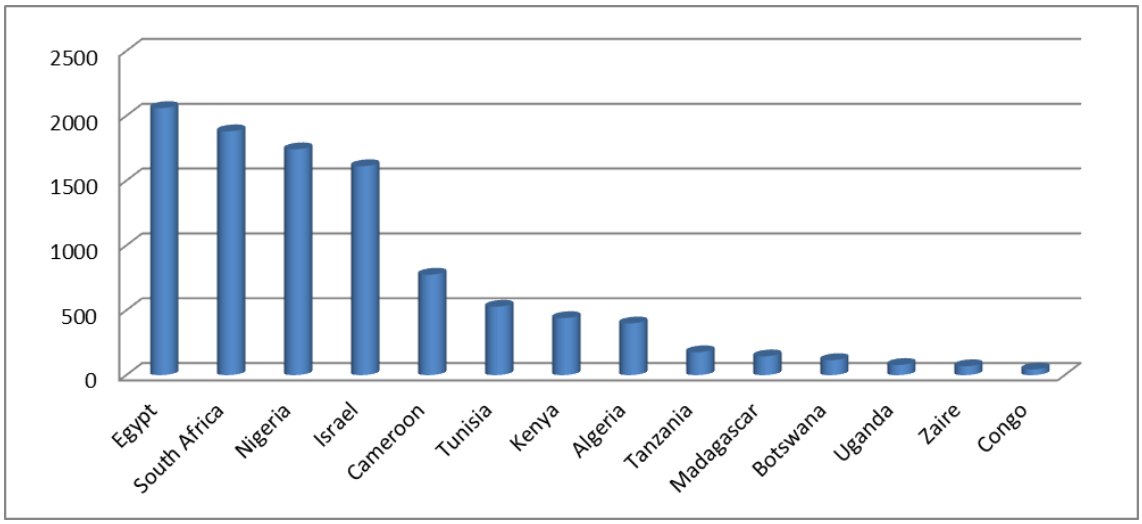
Africa

The last geographical region to be analyzed is Africa. The region has three countries with megabiodiversity, but takes part with 10,067 articles or less than 5%, of the total. Egypt and South Africa are the leaders with 2060 and 1881 articles, respectively. Israel, with the 16th position according to HDI, occupies the third place in the region and 35th in the world. (1.612 papers) (Tables 12, 13 and Graphic 5).

Table 8. Number of papers published by African countries, values and rank of HDI

Country	N^0 of papers	%	HDI	Rank
1. Egypt	2060	20,46	0.662	112nd
2. South Africa	1881	18,68	0.629	121st
3. Nigeria	1742	17,30	0.471	153rd
4. Israel	1612	16,01	0.900	16th
5. Cameroon	775	7,69	0,495	150th
6. Tunisia	528	5,24	0.713	93nd
7. Kenya	440	4,37	0.519	145th
8. Algeria	399	3,96	0.712	44th
9. Tanzania	177	1,75	0.713	93rd
10. Madagascar	145	1,44	0.483	151st
11. Botswana	116	1,15	0.634	119th
12. Uganda	79	0,78	0.456	160th

13. Zaire	69	0,68	0.304	186th
14. Congo	44	0,43	0.534	142nd
Total	10067			



Graphic 5. Number of papers published by African countries

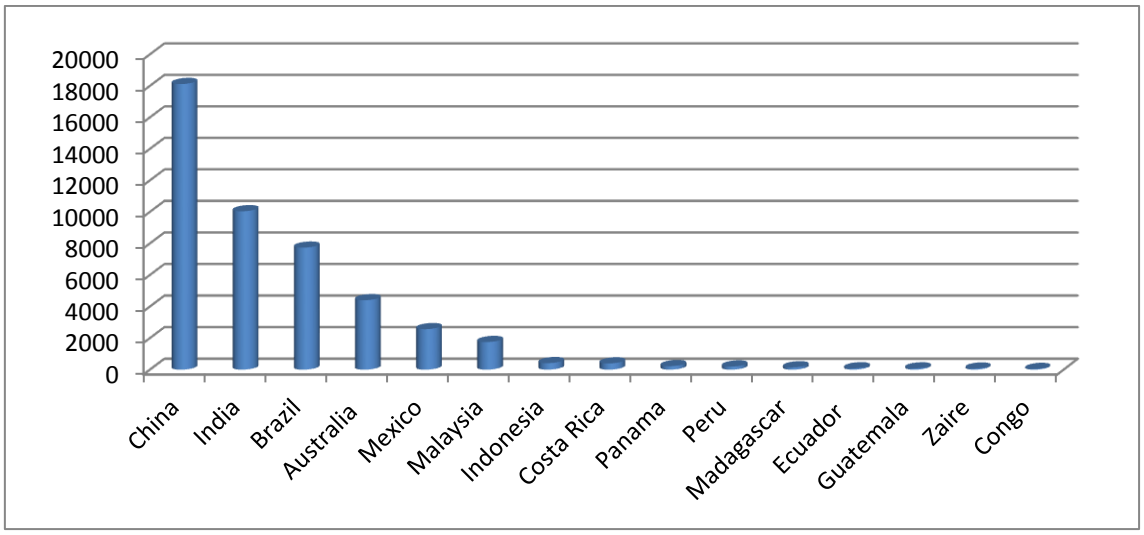
Countries with megabiodiversity

Finally, it is worth comparing the position of each country with a megabiodiversity. The 15 countries publish 46,253 articles, or 21.30% of the total. China occupies the first of the rank with 18,118 papers or almost 40% of the total. India is the second and Brazil the third, with 1040 and 7732 articles, respectively. Australia, the second in the rank of HDI, is the fourth position (Table 14 and Graphic 6).

Table 9. Number of articles published by the 15 countries with a megabiodiversity, their HDI and rank in HDI

Country	N^0 of papers	%	HDI	Rank in HDI
1. China	18118	39.17	0,669	101^0
2. India	10040	21,70	0,554	138^0
3. Brazil	7732	16,71	0,730	85^0
4. Australia	4401	9,51	0,938	2^0
5. Mexico	2568	5,55	0,775	61^0
6. Malaysia	1749	3,78	0,769	64^0
7. Indonesia	413	0,89	0,629	121^0
8. Costa Rica	394	0,85	0,780	59^0

9. Panama	223	0,48	0,773	62^0
10. Peru	197	0,42	0,741	77^0
11. Madagascar	145	0,31	0,483	151^0
12. Ecuador	83	0,17	0,724	89^0
13. Guatemala	77	0,16	0,581	133^0
14. Zaire	69	0,14	0,304	186^0
15. Congo	44	0,09	0,534	142^0
	46253			



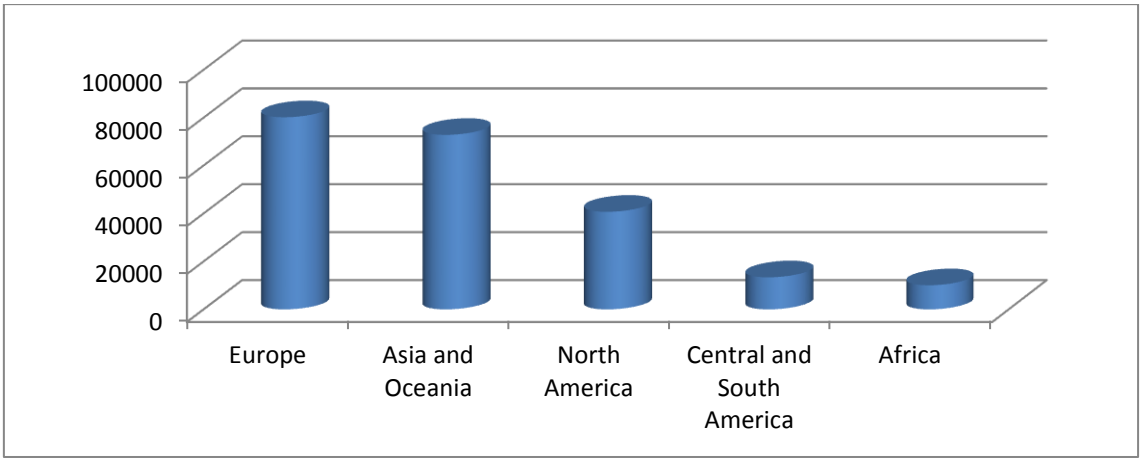
Graphic 6. Number of papers published by the 15 countries with megabiodiversity

Table 10 and Graphic 7 compare the number of megabiodiversity countries in each continent with that of papers published by them. They show that Europe and North America, with 29 selected countries and only one with megabiodiversity (Mexico), are responsible for more than half (55.65%) of all articles, while the other three continents with 41 countries and 14 with megabiodiversity produce the other 45%. Asia and Oceania, with 5 countries with megabiodiversity, respond for 33.3%. On the other hand, Central, South America and Caribbean (Cuba) and Africa, with 9 megabiodiversity countries, a little more than 10% of the total produced in the world.

Table 10. Comparison between the five continents with respect to number of papers published in the select journals

Continent	Number of countries	No of countries with megabiodiversity	Total of Articles
Europe	26	0	80156
Asia and Oceania	14	5	72800
North America	3	1	40693

Central and South America	13	6	13396
Africa	14	3	10067
Total	70	15	217112



Graphic 7. Comparison between the five continents with respect to number of papers published in the select journals

These data lead to a question: Is there any relationship between the number of papers published by a given country and its economic status?

To answer this question, it is necessary to compare both data.

5. Human Development Report

The Human Development Index[202] of each country was used in order to check the relationship of the economical and development index of each country with the numbers of articles published in the selected journals (Table 2). This Table shows 67 countries because North Ireland, Scotland, Wales and Taiwan do not appear in the Human Development Index of the World Bank. However, they were included in the list because they appear in the Thompson Institute list.

The origins of the HDI are found in the annual Development Reports of the United Nations Development Programme (UNDP). These were devised and launched by Pakistani economist Mahbubul Haq in 1990 and had the explicit purpose "to shift the focus of development economics from national income accounting to people-centered policies". HDI combines three dimensions:

-A long and healthy life: Life expectancy at birth

-Education index: Mean years of schooling and Expected years of schooling

-A decent standard of living.

The index ranks 186 countries by 4 categories as follows Table 11):

Table 11. Human Development Report Index

Development	N° of countries	HDI
Very high	47	0.955-0.805
High	47	0.769-0.712
Medium	46	0.710-0.536
Low	44	0.534-0.304

Table 3 shows that Norway occupies the first position with an HDI value of 0.955 (maximum is 1), but has a very modest position (41st) when the number of papers is considered (1028), while Zaire (now Democratic Republic of Congo) occupies the 186a position with an HDI of 0.304 and the 69th (among 70) with regard the number of articles (only 69).

The positions of the other countries with a megabiodiversity, runs from Mexico (18th position, 2.568 papers, and an HDI of 0.769) to Congo (70rd), 44 papers and a HDI 0.534).

However, Table 12 shows that 13 countries, among the 20 listed, are classified as very highly developed according to HDI, 1 as highly developed and 4 as medium. Moreover, all of them, except Sweden, also occupy the 20 first places according to the number of papers published (Sweden is the 21st) (see Table 3).

Table 12. Number of papers published by the 20 topic countries

Country	N0 of papers	N0 of citations	Citation per paper
1. USA	3,049,662	48,862,100	16.02
2. China	836,255	5,191,358	6.21
3. Germany	784,316	10,518,133	13.41
4. Japan	771,548	8,084,145	10.48
5. England	697,763	10,508,202	15.06
6. France	557,322	7,007,693	12.57
7. Canada	451,588	6,019,195	13.33
8. Italy	429,301	5,151,675	12.00
9. Spain	339,164	3,588,655	10.58
10. Australia	304,160	3,681,695	12.10
11. India	293,049	1,727,973	5.90
12. South Korea	282,328	2,024,609	7.17
13. Russia	265,721	1,282,281	4.83
14. Netherlands	252,242	3,974,719	15.76

15. Brazil	212,243	1,360,097	6.41
16. Switzerland	181,636	3,070,458	16.90
17. Sweden	179,126	2,686,304	15.00
18. Taiwan	177,929	1,273,682	7.16
19. Turkey	155,276	819,071	5.27
20. Poland	154,016	1,036,062	6.73

6. Conclusions and future perspectives

The data discussed in this paper show that, with few exceptions, scientific production in the areas of chemistry and pharmacology of natural products, presents a close relation with the HDI of each country.

The data also show that despite its place with regard to HDI, Brazil occupies a good situation, the ninth position in comparison with 70 countries of all geoGraphical regions. Its rank varies from the first place, when compared with Africa and Central and South America to the fifth in comparison with Europe (Table 12).

The articles published by the 15 countries with a megabiodiversity (Table 10) also deserve a comment. Europe is the only continent without any country in the group. Australia is the only country belonging to the highly developed world. Asia is represented by four countries two of which (China and India) occupy to high position concerning the number of papers published. In contrast, Africa appears with three countries two of which (Zaire and Congo) occupy the lowest position. Latin America has seven countries in the group with a quite variable position both in the number of papers published and concerning to their IDH.

The market for 'natural products', derived from plants and other living organisms (pigments, dyes, fragrances, aromas, flavors, cosmetics, perfumes, insecticides and medicines), is really remarkable.

Transformation of the knowledge accumulated up to now in this area, into commercial realities will take time. But the rational use Brazilian biological diversity represents a unique opportunity for the social, economic and technological development of the country.

Ackowledgements

We are in debt to Drs. Benjamin Gilbert, Antonio Carlos Siani and José Luiz Mazzei (Far-Manguinhos) for reading the manuscript and to Far-Manguinhos for financial assistance.

References

[1] Wilson, E. O. *The Current state of biological diversity. In Biodiversity*, in: Wilson, E.O., Peter, F.P. (Eds.*), The National Academy of Sciences*, Washington, **1988**.

[2] Fraenkel, G. S. The Raison d'Être of Secondary Plant Substances. *Science* **1959**, *129*, 1466. [CrossRef] [PubMed]

[3] Karlson, P.; Butenandt, A. Pheromones (Ectohormones) in Insects. *Annual Review of Entomology* **1959***, 4*, 39. [CrossRef]

[4] Law, J. H.; Regnier, F. E. Pheromones. *Annual Review of Biochemistry* **1971**, *40*, 533. [CrossRef]

[5] Whittaker, R. H.; Feeny, P. P. Allelochemics: Chemical Interactions between Species *Science* **1971**, *171*, 757. [CrossRef] [PubMed]

[6] Sondheimer, E.; Simeone, J. B. *Chemical ecology*. Academic Press, New York, 1970.

[7] Bohlin, L.; Göransson, U.; Alsmark, C.; Weden, C.; Backlund, A. Natural products in modern life science. *Phytochemistry Reviews* **2010**, *9,* 279. [CrossRef] [PubMed]
[8] Meinwald, J. The Chemistry of Biotic Interactions in Perspective: Small Molecules Take Center Stage *Journal of Organic Chemistry* **2009**, *74*, 1813. [CrossRef]
[9] Meinwald, J. Natural Products as Molecular Messengers. *Journal of Natural Products* **2011**, *74*, 305. [CrossRef]
[10] Ióca, L. P.; Allard, P. M.; Berlinck, R. G. S. Thinking big about small beings – the (yet) underdeveloped microbial natural products chemistry in Brazil. *Natural Product Reports* **2014**, *31*, 646. [CrossRef] [PubMed]
[11] Dunny, G. M. Enterococcal Sex Pheromones: Signaling, Social Behavior, and Evolution. *Annual Review of Genetics* **2013**, *47,* 457. [CrossRef] [PubMed]
[12] Groenhagen, U.; Baumgartner, R.; Baily, A.; Gardiner, A.; Eberl, L.; Schulz, S.; Weiskopf, L. Production of Bioactive Volatiles by Different *Burkholderia ambifaria* Strains. *Journal of Chemical Ecology* **2013**, *39,* 892. [CrossRef] [PubMed]
[13] Wasserstrom, L.; Lengeler, K. B.; Walther, A.; Wendland, J. Molecular Determination of Sporulation in *Ashbya gosspii. Genetics* **2013**, *195***,** 87. [CrossRef] [PubMed]
[14] Lyell, N. L.; Colton, D. M.; Bose, J. L.; Tumen-Velasquez, M. P.; Kimbrough, J. H.; Stabb, E. V. Cyclic AMP Receptor Protein Regulates Pheromone-Mediated Bioluminescence at Multiple Levels in *Vibrio fischeri* ES114 Journal *of Bacteriology* **2013**, *195,* 5051. [CrossRef] [PubMed]
[15] Citron, C. A.; Rabe, P.; Dickschat, J. S. The Scent of Bacteria: Headspace Analysis for the Discovery of Natural Products. *Journal of Natural Products* **2012**, *75,* 1765. [CrossRef]
[16] Nieuwenhuis, B. P. S.; Aanen, D. K. Sexual selection in fungi. *Journal of Evolutionary Biology* **2012**, *25*, 2397. [CrossRef] [PubMed]
[17] Woodley, S. Chemosignals, hormones, and amphibian reproduction.*Hormones and Behavior* **2015**, *68,* 3. [CrossRef] [PubMed]
[18] Starnberger, I.; Preininger, D.; Hödl, W. The anuran vocal sac: a tool for multimodal signaling. *Animal Behaviour* **2014**, *97,* 281. [CrossRef] [PubMed]
[19] Saporito, R. A.; Donnelly, M. A.; Spande, T. F.; Garraffo, H. M. A review of chemical ecology in poison frogs. *Chemoecology* **2012**, *22*, 159. [CrossRef]
[20] Poth, D.; Wollenberg, K. C.; Vences, M.; Schulz, S. Volatile Amphibian Pheromones: Macrolides from Mantellid Frogs from Madagascar. *Angewandte Chemie International Edition* **2012**, *51,* 2187. [CrossRef] [PubMed]
[21] Cummins, S. F.; Bowie, J. H. Pheromones, attractants and other chemical cues of aquatic organisms and amphibians. *Natural Product Reports* **2012**, *29*, 642. [CrossRef] [PubMed]
[22] Lutterschmidt, D. L.; Maine, A. R. Sex or candy? Neuroendocrine regulation of the seasonal transition from courtship to feeding behavior in male red-sided garter snakes (*Thamnophis sirtalis parietalis*). *Hormones and Behavior* **2014**, *66*, 120. [CrossRef] [PubMed]
[23] Fortes-Marco, L.; Lanuza, E.; Martinez-Garcia, F. Of Pheromones and Kairomones: What Receptors Mediate Innate Emotional Responses? *The Anatomical Record* **2013**, *296*, 1346. [CrossRef]
[24] Parker, M. R.; Mason, R. T. A novel mechanism regulating a sexual signal: The testosterone-based inhibition of female sex pheromone expression in garter snakes. *Hormones and Behavior* **2014**, *66*, 509. [CrossRef] [PubMed]
[25] Schulz, S. Spider Pheromones – a Structural Perspective. *Journal of Chemical Ecology* **2013**, *39*, 1. [CrossRef] [PubMed]
[26] Tedore, C.; Johnsen, S. Pheromones exert top-down effects on visual recognition in the jumping spider *Lyssomanes viridis*. *Journal of Experimental Biology* **2013**, *216,* 1744. [CrossRef] [PubMed]
[27] Font, E.; Barbosa, D.; Sampedro, C.; Carazo, P. Social behavior, chemical communication, and adult neurogenesis: Studies of scent mark function in *Podarcis* wall lizards. *General and Comparative Endocrinology* **2012**, *177,* 9. [CrossRef] [PubMed]

[28] Olsen, C. A.; Kristensen, A. S.; Strongaard, K. Small Molecules from Spiders Used as Chemical Probes. *Angewandte Chemie International Edition* **2011**, *50,* 11296. [CrossRef] [PubMed]
[29] Whittaker, D. J.; Gerlach, N. M.; Soini, H. A.; Novotny, M. V.; Ketterson, E. D. Bird odour predicts reproductive success. *Animal Behavior* **2013**, *86*, 697. [CrossRef]
[30] Campagna, S.; Mardon, J.; Celerier, A.; Bonadonna, F. Potential Semiochemical Molecules from Birds: A Practical and Comprehensive Compilation of the Last 20 Years Studies. *Chemical Senses* **2012**, *37*, 3. [CrossRef]
[31] Leclaire, S.; Merkling, T.; Raynaud, C.; Mulard, H.; Bessière, J. M.; Lhuillier, E.; Hatch, S.A.; Danchin, E. Semiochemical compounds of preen secretion reflect genetic make-up in a seabird species. *Proceedings of the Royal Society of London B: Biological Sciences* **2012**, *279*, 1185. [CrossRef]
[32] Mardon, J.; Saunders, S. M.; Anderson, M. J.; Couchoux, C.; Bonadonna, F. Species, Gender, and Identity: Cracking Petrels' Sociochemical Code. *Chemical Senses* **2010**, *35,* 309. [CrossRef]
[33] Caro, S. P.; Balthazart, J. Pheromones in birds: myth or reality? *Journal of Comparative Physiology* **2010**, *196,* 751. [CrossRef] [PubMed]
[34] Blunt, J. W.; Copp, B. R.; Keysers, R. A.; Munro, R. M. H. G.; Prinsep, M. R. Marine natural products. *Natural Product Reports* **2013**, *30,* 237. [CrossRef] [PubMed]
[35] Gerwick, W. H.; Fenner, A. M. Drug Discovery from Marine Microbes. *Microbial Ecology* **2013**, *65,* 800. [CrossRef] [PubMed]
[36] Leal, M. C.; Munro, M. H. G.; Blunt, J. W.; Puga, J.; Jesus, B.; Calado, R.; Rosa, R.; Madeira, C. Biogeography and biodiscovery hotspots of macroalgal marine natural products. *Natural Product Reports* **2013**, *30*, 1380. [CrossRef] [PubMed]
[37] Roy, J. S.; Poulson-Ellestad, K. L.; Sieg, R. D.; Poulin, R. X.; Kubanek, J. Chemical ecology of the marine plankton. *Natural Products Reports* **2013**, *30,* 1364. [CrossRef] [PubMed]
[38] Gerwick, W. H.; Moore, B. S. Lessons from the Past and Charting the Future of Marine Natural Products Drug Discovery and Chemical Biology. *Chemistry & Biology* **2012**, *19*, 85. [CrossRef] [PubMed]
[39] Leal, M. C.; Puga, J.; Seródio, J.; Gomes, N. M. C.; Calado, R. Trends in the Discovery of New Marine Natural Products from Invertebrates over the Last Two Decades – Where and What Are We Bioprospecting? *PlosOne* **2012**, *7, e30580.* [CrossRef] [PubMed]
[40] Leão, P. N.; Engene, N.; Antunes, A.; W. H. Gerwick, W. H.; Vasconcelos, V. The chemical ecology of cyanobacteria. *Natural Product Reports* **2012**, *29*, 372. [CrossRef][PubMed]
[41] Blunt, J. W.; Copp, B. R.; Keysers, R. A.; Munro, M. H. G.; Prinsep, M. R. Marine natural products. *Natural Product Reports* **2012**, *29,* 144. [CrossRef][PubMed]
[42] Liberles, D. S. Mammalian Pheromones. *Annual Revew of Physiology* **2014**, *76,* 151. [CrossRef][PubMed]
[43] Schaal, B; Ain, S. A. Chemical signals 'selected for' newborns in mammals. *Animal Behaviour* **2014**, *97,* 289. [CrossRef]
[44] Petrulis, A. Chemosignals, hormones and mammalian reproduction. *Hormones and Behavior* **2013**, *63,* 723. [CrossRef] [PubMed]
[45] Petrulis, A. Chemosignals and hormones in the neural control of mammalian sexual behavior. *Frontiers in Neuroendocrinology* **2013**, *34,* 255. [CrossRef] [PubMed]
[46] Baum, M. J.; Bakker, J. Roles of sex gonadal steroids in mammalian pheromonal communication. *Frontiers in Neuroendocrinology* **2013**, *34*, 268. [CrossRef] [PubMed]
[47] Buissonnière-Ariza, V.; Lepore, F.; Kojok, K. M.; Frasnelli, J. Increased Odor Delection Speed in Highly Anxious Healthy Adult. *Chemical Senses* **2013**, *38*, 577. [CrossRef] [PubMed]
[48] Derntl, B.; Schöpf, V.; Kollndorfer, K.; Lanzenberger, R. Menstrual Cycle Phase and Duration of Oral Contraception Intake Affect Olfactory Perception. *Chemical Senses* **2013**, *38*, 67. [CrossRef] [PubMed]
[49] Dormont, L.; Bessière, J. M.; Cohuet, A. Human Skin Volatiles: A Review. *Journal of Chemical Ecology* **2013**, *39*, 569. [CrossRef] [PubMed]
[50] Knaapila, A.; Hwang, L. D.; Lysenko, A.; Duke, F. F.; Fesi, B.; Khoshnevisan, A.; James,

R. S.; Wysocki, C. J.; Rhyu, M. R.; Tordoff, M. G.; Bachmanov, A. A.; Mura, E.; Nagai, H.; Reed, D. R. Genetic Analysis of Chemosensory Traits in Human Twins. *Chemical Senses* **2012**, *37,* 869. [CrossRef] [PubMed]

[51] Lapid, H.; Hummel, T. Recording Odor-Evoked Response Potential at the Human Olfactory Epithelium. *Chemical Senses* **2013**, *38*, 3. [CrossRef] [PubMed]

[52] McGann, J. P. Presynaptic Inhibition of Olfactory Sensory Neurons: New Mechanisms and Potential Functions. *Chemical Senses* **2013**, *38,* 459. [CrossRef] [PubMed]

[53] Palouzier-Paulignan, B.; Lacroix, M. C.; Aimé, P.; Baly, C.; Caillol, M.; Congar, P.; Julliard, A.K.; Tucker, K.; Fadool, D.A. Olfaction Under Metabolic Influences. *Chemical Senses* **2012**, *37,* 769. [CrossRef] [PubMed]

[54] Verpoorte, R. *Overview and introduction*. In: Wander, L., Liu, H.W. (Eds.), *Comprehensive natural products*, II. v. 3. 1st edition. Elsevier, London/New York, pp. 1. **2010**.

[55] Kupferschmidt, K. From Toxins to Treatment. *Science,* **2013**, *342,* 1162. [CrossRef]

[56] Saez, N.J.; Senff, S.; Jensen, J.E.; Er, S.Y.; Herzig, V.; Rash, L.D.; King, G.F. Spider-Venom Peptides as Therapeutics. *Toxins*, **2010**, *2,* 2851. [CrossRef] [PubMed]

[57] Clark, V. C.; Harinantenaina, L.; Zeller, M.; Ronto, W.; Rocca, J.; Dossey, A. T.; Rakotondravony, D.; Kingston, D. G. I.; Shaw, C. An Endogenous Bile Acid and Dietary Sucrose from Skin Secretions of Alkaloid-Sequestering Poison Frogs. *Journal of Natural Products* **2012**, *75,* 473. [CrossRef] [PubMed]

[58] Alves, L. F. *Plantas Medicinais e Fitoquímica no Brasil: Uma Visão Histórica*, 1st ed. Pharmabooks, São Paulo. **2010**.

[59] Zarshenas, M. M.; Zargaram, A. A review on the Avicena's contribution to the field of cardiology. *International Journal of Cardiology* **2015**, *182,* 237. [CrossRef] [PubMed]

[60] Gänger, S. World Trade in Medicinal Plants from Spanish America, 1715-1815. *Medical History* **2015**, *59,* 44. [CrossRef] [PubMed]

[61] Khan, H. Medicinal Plants in Light of History: Recognized Therapeutic Modality. *Journal of Evidence Based Complementary & Alernative Medicine* **2014**, *19*, 216. [CrossRef] [PubMed]

[62] Alves, L. F. Produção de Fitoterápicos no Brasil: História, Problemas e Perspectivas. *Revista Virtual de Química* **2013**, *5,* 450. [CrossRef]

[63] Alves, L. F.; Santos, P. F. P. Brazilian biodiversity as a source of new medicines. *Brazilian Journal of Pharmacy* **2013***, 94,* 307. [Link]

[64] Hamedi, A.; Zarshenas, M. M.; Sohrabpour, M.; Zargaran, A. Herbal medicinal oils in traditional Persian medicine. *Pharmaceutical Biology* **2013**, *51,* 1208. [CrossRef] [PubMed]

[65] Adams, M.; Schneider, S. V.; Kluge, M.; Kessler, M.; Hamburger, M. Epilepsy in the Renaissance: A survey of remedies from 16th and 17th century German herbals. *Journal of Ethnopharmacology* **2012**, *143,* 1. [CrossRef] [PubMed]

[66] Pérez-Arantegui, J.; Ribechini, E.; Colombini, M. P.; Escudero, F. Characterization of an ancient 'chemical' preparation: pigments and drugs in medieval Islamic Spain. *Journal of Archaelogical Science* **2011**, *38,* 3350. [CrossRef]

[67] Giachi, G.; Pallecchi, P.; Romualdi, A.; Ribechini, E.; Lucejko, J. J. Colombini, M. P.; Lippi, M. M. Ingredients of a 2,000-y-old medicine revealed by chemical, mineralogical, and botanical investigation. *Proceedings of the National Academy of Sciences* **2012**, *110,* 1193. [CrossRef] [PubMed]

[68] Stacey, R. J. The composition of some Roman medicines: evidence for Pliny's Punic wax? *Analytical and Bioanalytical Chemistry* **2011**, *401,* 1749. [CrossRef] [PubMed]

[69] Hardy, K.; Buckley, S.; Collins, M. J.; Estalrrich, A.; Brothwell, D.; Copeland, L.; Garcia-Tabernero, A.; Garcia-Vargas, S.; de la Rastilla, M.; Lalueza-Fox, C.; Huguet, R.; Bastir, M.; Santamaría, D.; Madella, M.; Wilson, J.; Cortés, A. F.; Rosas, A. Neanderthal medics? Evidence for food, cooking, and medicinal plants entrapped in

dental calculus. *Naturwissenhaften* **2012**, *99,* 617. [CrossRef] [PubMed]
[70] Bouin, A. S.; Wierer, M. Quality standards of the European Pharmacopoeia. *Journal of Ethnopharmacology* **2014**, *158,* 454. [CrossRef] [PubMed]
[71] Bilia, A. R. Science meets regulation. *Journal of Ethnopharmacology* **2014**, *158,* 487. [CrossRef] [PubMed]
[72] Shikov, A. N.; Pozharitskaya, O. N.; Makarov, V. G.; Wagner, H.; Verpoorte, R.; Heinrich, M. Medicinal plants of the Russian Pharmacopoeia; their history and applications. *Journal of Ethnopharmacology* **2014**, *154,* 481. [CrossRef] [PubMed]
[73] Naghibi, F.; Khalaj, A.; Mosaddegh, M.; Malekmohamadi, M; Hamzeloo-Moghadan, M. Cytotoxic activity evaluation of some medicinal plants, selected from Iranian traditional medicine Pharmacopoeia to treat cancer and related disorders. *Journal of Ethnopharmacology* **2014**, *155,* 230. [CrossRef] [PubMed]
[74] Albuquerque, U. P.; Medeiros, P. M.; Ramos, M. A.; Ferreira Jr., W. S.; Nascimento, A. L. B.; Avilez, W. M. T.; Melo, J. G. Are ethnopharmacological surveys useful for the discovery and development of drugs from medicinal plants? *Brazilian Journal of Pharmacognosy* **2014**, *24,* 110. [CrossRef]
[75] Pascolutti, M.; Quinn, R. J. Natural products as lead structures: chemical transformations to create lead-like libraries. *Drug Discovery Today* **2014**, *19,* 215. [CrossRef] [PubMed]
[76] Bauer, A.; Brönstrup, M. Industrial natural products chemistry for drug discovery and development. *Natural Product Reports* **2014**, *31,* 35. [CrossRef] [PubMed]
[77] Simpson, B. S.; Claudie, D. J.; Smith, N. M.; McKinnon, R. A.; Semple, S. J. Learning from Both Sides: Experiences and Opportunities in the Investigation of Australian Aboriginal Medicinal Plants. *Journal of Pharmacy & Pharmaceutical Sciences* **2013**, *16,* 259. [CrossRef] [PubMed]
[78] Niemeyer, K.; Bell, I. R.; Koithan, M. Traditional knowledge of Western herbal medicine and complex system science. *Journal of Herbal Medicine* **2013**, *3,* 112. [CrossRef] [PubMed]
[79] Ngo, L. T.; Okogun, J. I.; Folk, W. R. 21st Century natural products research and drug development and traditional medicines. *Natural Product Reports* **2013**, *30,* 584. [CrossRef] [PubMed]
[80] Leonti, M.; Cabras, S.; Castellanos, M. E.; Challenger, A.; Gertsch, J.; Casu, L. Bioprospecting: Evolutionary implications from a post-olmec pharmacopoeia and the relevance of widespread taxa. *Journal of Ethnopharmacology,* **2013**, *147,* 92. [CrossRef] [PubMed]
[81] Hur, M.; Campbell, A. A.; Almeida-de-Macedo, M.; Ling, L.; Ransom, N.; Jose, A.; Crispin, M.; Nikolau, B. J.; Wurtele, E. S. A global approach to analysis and interpretation of metabolic data for plant natural product discovery. *Natural Product Reports* **2013**, *30,* 565. [CrossRef] [PubMed]
[82] Cragg, G. M.; Newman, D. J. Natural products: A continuing source of novel drug leads. *Biochimica et Biophysica Acta* **2013**, *1830,* 3670. [CrossRef] [PubMed]
[83] Bucar, F.; Wube, A.; Schmid, M. Natural product isolation – how to get from biological material to pure compounds. *Natural Product Reports* **2013**, *30,* 525. [CrossRef] [PubMed]
[84] Valli, M.; Pivatto, M.; Danuello, A.; Castro-Gamboa, I.; Silva, D. H. S.; Cavalheiro, A. J.; Araújo, A. R.; Furlan, M.; Lopes, M. N. Bolzani, V. S. Tropical Biodiversity: Has It Been a Potential Source of Secondary Metabolites Useful for Medicinal Chemistry? *Química Nova* **2012**, *35,* 2278. [CrossRef]
[85] Newman, D. J.; Cragg, G. M. Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010. *Journal of Natural Products* **2012,** *75,* 311. [CrossRef] [PubMed]
[86] Cordell, G. A.; Colvard, M. D. Natural Products and Traditional Medicine: Turning on a Paradigm. *Journal of Natural Products* **2012**, *75,* 514. [CrossRef] [PubMed]
[87] Sawadogo, W. R.; Schumacher, M.; Teiten, M. H.; Dicato, M.; Dietrich, D. Traditional West African pharmacopoeia, plants and derived compounds for cancer therapy. *Biochemical Pharmacology* **2012**, *84,* 1225. [CrossRef] [PubMed]
[88] Bolzani, V. S.; Valli, M.; Pivatto, M.; Viegas Jr., C. Natural products from Brazilian

biodiversity as a source of new models for medicinal chemistry. *Pure and Applied Chemistry* **2012***, 84***,** 1837. [CrossRef]

[89] Moura, G. J. B.; Albuquerque, U. P. The First Report on the Medicinal Use of Fossils in Latin America. *Evidence Based Complementary and Alternative Medicine*, article ID 691717, **2012**. [CrossRef] [PubMed]

[90] Maffei, M. E.; Gertsch, J.; Appendino, G. Plant volatiles: Production, function and pharmacology. *Natural Product Reports* **2011**, *28,* 1359. [CrossRef] [PubMed]

[91] Kingston, D. G. I. Modern Natural Products Drug Discovery and Its Relevance to Biodiversity Conservation. *Journal of Natural Products* **2011**, *74,* 496. [CrossRef] [PubMed]

[92] Kinghorn, A. D.; Pan, L.; Fletcher, J. N.; Chai, H. B. The Relevance of Higher Plants in Lead Compound Discovery Programs. *Journal of Natural Products* **2011**, *74,* 1539. [CrossRef] [PubMed]

[93] Cordell, G. A. Sustainable Medicines and Global Health Care. *Planta Medica* **2011**, *77,* 1129. [CrossRef] [PubMed]

[94] Carter, G. T. Natural products and Pharma 2011: Strategic changes spur new opportunities. *Natural Product Reports* **2011**, *28,* 1783. [CrossRef] [PubMed]

[95] Vos, P. D. European material medica in historical texts: Longevity of a tradition and implications for future use. *Journal of Ethnopharmacology* **2010**, *132,* 28. [CrossRef] [PubMed]

[96] Egan, P. A.; Kooy, F. Phytochemistry of the Carnivorous Sundew Genus *Drosera* (Droseraceae) – Future Perspective and Ethnopharmacological Relevance. *Chemistry & Biodiversity* **2013**, *10,* 1774. [CrossRef] [PubMed]

[97] Hossain, M. M. Therapeutic orchids: traditional uses and recent advances – An overview. *Fitoterapia* **2011**, *82,* 102. [CrossRef] [PubMed]

[98] Sakai, R.; Swanson, G.T. Recent progress in neuroactive marine natural products. *Natural Product Reports* **2014**, *31,* 273. [CrossRef] [PubMed]

[99] Luo, L.; Wu, M. Y.; Xu, L.; Lian, W.; Xiang, J. Y.; Lu, F.; Gao, N.; Xiao, C.; Wang, S. G.; Zhao, J. H. Comparison of Physicochemical Characteristics and Anticoagulant Activities of Polysaccharides from Three Sea Cucumbers. *Marine Drugs* **2013**, *11,* 399. [CrossRef] [PubMed]

[100] Abida, H.; Ruchaud, S.; Rios, L.; Humeau, A.; Probert, I.; Vargas, C.; Bach, S.; Bowler, C. Bioprospecting Marine Plankton. *Marine Drugs* **2013**, *11,* 4594. [CrossRef] [PubMed]

[101] Spavieri, J.; Allmendinger; Kaiser, M. Itoe, A. M.; Blunden, G.; Mota, M. M.; Tasdemir, D. Assesment of Dual Life Stage Antiplasmodial Activity of British Seaweeds. *Marine Drugs* **2013**, *11,* 4019. [CrossRef] [PubMed]

[102] Senthilkumar, K.; Kim, S. K. Marine Invertebrate Natural Products for Anti-Inflammatory and Chronic Diseases. *Evidence Based Complementary and Alternative Medicine*, article ID 572859, **2013**. [CrossRef] [PubMed]

[103] Sawadogo, W. R.; Schumacher, M.; Teiten, M. H.; Cerella, C.; Dicato, M.; Diederich, M. A Survey of Marine Natural Compounds and Their Derivatives with Anti-Cancer Activity Reported in 2011. *Molecules* **2013**, *18,* 3641. [CrossRef] [PubMed]

[104] Liu, J. T.; Lu, X. L.; Liu, X. Y.; Gao, Y.; Hu, B.; Jiao, B. H.; Zheng, H. Bioactive Natural Products from the Antartic and Artic Organims. *Mini Review in Medicinal Chemistry* **2013**, *13,* 617. [CrossRef] [PubMed]

[105] Pozharitskaya, O. N.; Shikov, A. N.; Makarova, M. N.; Ivanova, S. A.; Kosman, V. M.; Makarov, V. G.; Bazgier, V.; Berka, K.; Otyepka, M.; Ultrichová, J. Antiallergic Effects of Pigments Isolated from Green Sea Urchin (*Strongylocentrotus droebachiensis*) Shells. *Planta Medica* **2013**, *79,* 1698. [CrossRef] [PubMed]

[106] Lin, M. C.; Pan, C.Y.; Hui, C. F.; Chen, J. Y.; Wu, J. L. Shrimp anti-lipopolysaccharide factor (SALF), an antimicrobial peptide, inhibits proinflammatory cytokine through the MAPK and NF-kB pathways in PLS-induced HeLa cells. *Peptides* **2013**, *40,* 42. [CrossRef] [PubMed]

[107] Pejin, B.; Jovanovic, K. K.; Mojovic, M.; Savic, A. G. New and Highly Potent Antitumor Natural Products from Marine-Derived Fungi: Covering the Period from 2003 to 2012.

Current Topics in Medicinal Chemestry **2013**, *13,* 2745. [CrossRef] [PubMed]
[108] Jones, A. J.; Grkovic, T.; Sykes, M. L.; Avery, V. Trypanocidal Activity of Marine Natural Products. *Marine Drugs* **2013**, *11,* 4058. [CrossRef] [PubMed]
[109] Manivasagan, P.; Venkatesan, J.; Sivakumar, K.; Kim, S. W. Marine actinobacterial metabolites: Current status and future perspective. *Microbiological Ressearch* **2013**, *168*, 311. [CrossRef] [PubMed]
[110] Fedorov, S. N.; Ermakova, S. P.; Zvyagintseva, T. N.; Stonik, V. A. Anticancer and Cancer Preventive Properties of Marine Polysaccharides: Some Results and Prospects. *Marine Drugs* **2013**, *11,* 4876. [CrossRef] [PubMed]
[111] López-Saiz, C. M.; Suárez-Jimenez, G. M.; Plascencia-Jatomea, M.; Burgos-Hernandez, A. Shrimp Lipids: A Source of Cancer Chemopreventive Compounds. *Marine Drugs* **2013**, *11*, 3926. [CrossRef] [PubMed]
[112] Bianco, E. M.; Oliveira, S. Q.; Rigotto, C.; Tonini, M. L.; Guimarães, T. R.; Bittencourt, F.; Gouvêa, L. P.; Aresi, C.; Almeida, M. T. R.; Moritz, M. I. G.; Martins, C. D. L.; Scherner, F.; Carraro, J. L.; Horta, P. A.; Reginatto, F. H.; Steindel, M.; Simões, C. M. O.; Schenkel, E. P. Anti-Infective Potential of Marine Invertebrates and Seaweeds from the Brazilian Coast. *Molecules* **2013**, *18,* 5761. [CrossRef] [PubMed]
[113] Suarez-Jimenez, G. M.; Burgos-Hernandez, A.; Ezquerra-Brauer, J. M. Bioactive Peptides and Depsipetides with Anticancer Potential: Source from Marine Animals. *Marine Drugs* **2012,** *10,* 963. [CrossRef] [PubMed]
[114] Yano, A.; Abe, A.; Aizawa, F.; Yamada, H.; Minami, K.; Matsui, M.; Kishi, M. The Effect of Eating Sea Cucumber Jelly on *Candida* Load in the Oral Cavity of Elderly Individuals in a Nursing Home. *Marine Drugs* **2013**, *11,* 4993. [CrossRef] [PubMed]
[115] Zhou, X. F.; Liu, J.; Yang, B.; Lin, X.; Yang, X. W.; Liu, Y. Marine natural products with anti-HIV activities in the last decade. *Current Medicinal Chemistry* **2013**, *20,* 953. [CrossRef] [PubMed]
[116] Kitahashi, T.; Ikawa, S.; Sakamoto, A.; Nomura, Y.; Tsujiuchi, T.; Shmizu, K.; Sasabe, S.; Park, E. Y.; Nakamura, Y.; Tsutsumi, M.; Sato, K. Ingestion of Proteoglycan Fraction from Shark Cartilage Increases Serum Inhibitory Activity against Matrix Metalloproteinase-9 and Suppresses Development of *N*-NItrosobis(2-oxopropyl)amine-Induced Pancreatic Duct Carcinogenesis in Hamster. *Journal of Agricultural and Food Chemistry* **2012**, *60*, 940. [CrossRef] [PubMed]
[117] Pampanin, D. A.; Larssen, E.; Provan, F.; Sivertsvik, M.; Ruolf, P.; Sydners, M. O. Detection of small bioactive peptides from the Atlantic herring (*Clupea harengus* L.). *Peptides* **2012**, *34,* 423. [CrossRef] [PubMed]
[118] Oliveira, A. L. L.; Felicio, R.; Debonsi, H. M. Marine natural products: chemical and biological potential of seaweeds and their endophytic fungi. *Brazilian Journal of Pharmacognosy* **2012**, *22,* 906. [CrossRef]
[119] Frota, Jr. M. L. C.; Silva, R. B.; Mothes, B.; Henriques, A. T.; Moreira, J. C. F. Current Status on Natural Products with Antitumor Activity from Brazilian Marine Sponges. *Current Pharmaceutical Biotechnology* **2012**, *13,* 235. [CrossRef] [PubMed]
[120] Cooper, E. L.; Yao, D. Diving for drugs: tunicate anticancer compounds. *Drug Discovery Today* **2012**, *17,* 636. [CrossRef] [PubMed]
[121] Hughes, C. C.; Fenical, W. Antibacterial from the Sea. *Chemistry:* **2010**, *16,* 12512. [PubMed]
[122] Voultsiadou, E. Therapeutic properties and uses of marine invertebrates in the ancient Greek world and early Byzantium. *Journal of Ethnopharmacology* **2010**, *130,* 237. [CrossRef] [PubMed]
[123] Schmeda-Hirschman, G.; Delpore, C.; Valenzuela-Barra, G.; Silva, X.; Vargas-Arana, G.; Lima, B.; Feresin, G. E. Anti-inflammatory activity of animal oils from the Peruvian Amazon. *Journal of Ethnopharmacology* **2014**, *156,* 9. [CrossRef] [PubMed]
[124] Koeppen, D.; Aurich, M.; Rampp, T. Medicinal leech therapy in pain syndromes: a narrative review. *Wien Medizisnische Wochenschrift* **2014**, *164,* 95. [CrossRef] [PubMed]
[125] Abdualkader, A.; Ghawi, A.; Alaama, M.; Awang, M. Merzouk, A. Leech Therapeutic

Applications. *Indian Journal of Pharmaceutical Sciences* **2013**, *75,* 127. [PubMed]

[126] Cherniak, E. P. Bugs as Drugs, Part Two: Worms, Leeches, Scorpions, Snails, Ticks, Centipedes, and Spiders. *Alternative Medicine Review* **2011**, *16,* 50 [PubMed]

[127] Stajic, M.; Vukojevic, J.; Knezevic, A. K.; Lausevic, S. D.; Milovanovic, I. Antioxidant Protective Effects of Mushroom Metabolites. *Current Topics in Medicinal Chemistry* **2013**, *13,* 2660. [CrossRef] [PubMed]

[128] Popovic, V.; Zivkovic, J.; Davidovic, S.; Stevanovic, M.; Stojkovic, D. Mycotherapy of Cancer: An Update on Cytotoxic and Antitumor Activities of Mushrooms, Bioactive Principles and Molecular Mechanisms of their Action. *Current Topics in Medicinal Chemistry* **2013**, *13,* 2791. [CrossRef] [PubMed]

[129] Alves, M. J.; Ferreira, I. C. F. R.; Dias, J.; Teixeira, V.; Martins, A.; Pintado, M. A Review on Antifungal Activity of Mushroom (Basidiomycetes) Extracts and Isolated Compounds. *Current Topics in Medicinal Chemistry* **2013**, *13,* 2648. [CrossRef] [PubMed]

[130] Alves, M. J.; Ferreira, I. C. F. R.; Teixeira, V.; Martins, A.; Pintado, M. A Review on Antimicrobial Activity of Mushroom (Basidiomycetes) Extracts and Isolated Compounds. *Planta Medica* **2012**, *78,* 1707. [CrossRef] [PubMed]

[131] Rathee, S.; Rathee, D.; Rathee, D.; Kumar, V.; Rathee, P. Mushrooms as therapeutic agents. *Brazilian Journal of Pharmacognosy* **2012**, *22,* 459. [CrossRef]

[132] Calcul, L.; Waterman, C.; Ma, W. S.; Lebar, M. D.; Harter, C.; Mutka, T.; Morton, L.; Maigan, P.; van Olphen, A.; Kyle, D. E.; Vrijmoed, L.; Pang, K.L.; Pearce, C.; Baker, B. J. Screening Mangrove Endophytic Fungi for Antimalarial Natural Products. *Marine Drugs,* **2013**, *11,* 5036. [CrossRef] [PubMed]

[133] Chandra, S. Endophytic fungi: novel sources of anticancer lead molecules. *Applied Microbiology and Biotechnology* **2012**, *95,* 47. [CrossRef] [PubMed]

[134] Gutierrez, R. M. P.; Gonzales, A. M. N.; Ramirez, A. M. Compounds Derived from Endophytes: A Review of Phytochemistry and Pharmacology. *Current Medicinal Chemistry* **2012**, *19,* 2992. [CrossRef] [PubMed]

[135] Radic, N.; Strukelj, B. Endophytic fungi – The treasure chest of antibacterial substances. *Phytomedicine* **2012**, *19,* 1270. [CrossRef] [PubMed]

[136] Jalgaonwala, R. E.; Moshite, B. V.; Maahajan, R. T. A review: Natural products from plant associated endophytic fungi. *Journal of Microbiology and Biotechnology Research* **2011**, *1,* 21. [Link]

[137] Bisset, N. One man's poison, another man's medicine? *Journal of Ethnopharmacology* **1991**, *32,* 71. [CrossRef] [PubMed]

[138] Harvey, A. L. Toxins and drug discovery. *Toxicon* **2014**, *92,* 193. [CrossRef] [PubMed]

[139] Baron, A.; Diochot, S.; Salinas, M.; Deval, E.; Noël, J.; Lingueglia, E. Venom toxins in the exploration of molecular physiological and pathophysiological functions of acid-sensing ion channels. *Toxicon* **2013**, *75,* 187. [CrossRef] [PubMed]

[140] Abrams, S. B.; Hallett, M. Clinical utility of different botulinum neurotoxin preparations. *Toxicon* **2013**, *67,* 81. [CrossRef] [PubMed]

[141] Heinen, T. E.; Veiga, A. B. G. Arthropod venoms and cancer. *Toxicon* **2011**, *57,* 497. [CrossRef] [PubMed]

[142] King, G. F. Venoms as a platform for human drugs: translating toxins into therapeutics. *Expert Opinion on Biological Therapy* **2011**, *11,* 1469. [CrossRef] [PubMed]

[143] Lima, M. E. (ed). *Animal Toxins: State of the Art. Perspective in Health and Biotechnology,* 1st ed., Editora da Universidade Federal de Minas Gerais, Belo Horizonte, **2009**.

[144] Cherniak, E. P. Bugs as Drugs, Part 1: Insects, The "New" Alternative Medicine for the 21st Century? *Alternative Medicine Review* **2010**, *15,* 124. [PubMed]

[145] Dossey, A. T. Insects and their chemical weaponry: New potential for drug discovery. *Natural Product Reports* **2010**, *27,* 1737. [CrossRef] [PubMed]

[146] De la Cruz, M. N. S.; Junior, M. S. H.; Oliveira, D. F.; Costa-Lotufo, L. V.; Ferreira, A. G.; Alviano, D. S.; Rezende, C. M. Chemical Composition and Biological Activities of

Soldiers of the Brazilian termite Species. *Nasutitermes microcephalus. Natural Product Communications* **2013**, *8,* 69. [PubMed]

[147] Moreau, S. J. M. "It stings a bit but it cleans well". Venoms of Hymenoptera and their antimicrobial potential. *Journal of Insect Physiology* **2013**, *59,* 186. [CrossRef] [PubMed]

[148] Harrison, P. L.; Abdel-Rahman, M. A.; Miller, K.; Strong, P. N. Antimicrobial peptides from scorpion venoms. *Toxicon,* **2014**, *88,* 115. [CrossRef] [PubMed]

[149] González, J. A.; Vallejo, J. R. The scorpion in Spanish folk medicine: A review of traditional remedies for stings and its use as a therapeutic resource. *Journal of Ethnopharmacology* **2013**, *146,* 62. [CrossRef] [PubMed]

[150] Rates, B.; Verano-Braga, T.; Santos, D. M.; Nunes, K. P.; Pimenta, A. M. C.; Lima, M. E. From the Stretcher to the Pharmacy's Shelf: Drugs Leads from Medically Important Brazilian Venomous Arachnid Species. *Inflammation & Allergy - Drug Targets* **2011**, *10,* 411. [CrossRef] [PubMed]

[151] Lima, M. E.; Borges, M. H.; Verano-Braga, T.; Torres, F. S.; Montadon, G. G.; Cardoso, F. L.; Peixoto, K. D. B. A.; Cardoso Jr., H. C.; Benelli, M. T. Some arachnidan peptides with potential medical application. *Journal of Venomous Animal Toxins including Tropical Diseases* **2010**, *16,* 8. [CrossRef]

[152] Costa, T. R.; Burin, S. M.; Menaldo, D. L.; Castro, F. A.; Sampaio, S. V. Snake venom L-aminoacid oxidase: an overview on their antitumor effects. *Journal of Venomous Animal Toxins including Tropical Diseases* **2014**, *20,* 23. [CrossRef] [PubMed]

[153] Vyas, V. K.; Brahmbhatt, K.; Bhatt, H.; Pamar, U. Therapeutic potential of snake venom in cancer therapy: current perspectives. *Asian Pacific Journal of Tropical Biomedicine* **2013**, *3,* 156. [CrossRef] [PubMed]

[154] Jain, D.; Kumar, S. Snake Venom: A Potential Anticancer Venom. *Asian Pacific Journal of Cancer Prevention* **2012**, *13,* 4855. [CrossRef] [PubMed]

[155] Koh, C. Y.; Kini, R. M. From snake venom toxins to therapeutics – Cardiovascular examples. *Toxicon* **2012**, *59,* 497. [CrossRef] [PubMed]

[156 156] Conlon, J. M.; Mechkarska, M.; Lukic, L.; Flatt, P. R. Potential therapeutic applications of multifunctional host-defense peptides from frog skin as anti-cancer, anti-viral, immunomodulatory, and anti-diabetic a gents. *Peptides* **2014**, *57*, 67. [CrossRef] [Pub,Med]

[157 157] Kouba, A. J.; Loyd, R. E.; Houck, M. L.; Silla, A. J.; Calatayud, N.; Trudeau, V. L.; Clulow, J.; Molinia, F.; Langhorne, C.; Vance, C.; Arregui, L.; Germano, J.; Lermen, D.; Togna, G. D. Emerging trends for biobanking amphibian genetic resources: The hope, reality and challenges for the next decade. *Biological Conservation* **2013**, *164,* 10. [CrossRef]

[158 158] Bazaz, M. R.; Mashreghi, M.; Shahri, M.N.; Mashreghi, M.; Assodeh, A.; Rassouli, M. B.; Golmohammadzadeh, S. Pharmaceutical application of frog skin on full-thickness skin wound healing in mice. *Pharmaceutical Biology* **2013**, *51,* 1600. [CrossRef] [PubMed]

[159 159] King, G. F.; Hardy, M. Spider-Venom Peptides: Structure, Pharmacology, and Potential for Control of Insect Pests. *Annual Review of Entomology* **2013**, *58,* 475. [CrossRef] [PubMed]

[160 160] Gomes, S. C.; Leonor, I. B.; Mano, J. F.; Reis, R. L.; Kaplan, D. L. Antimicrobial functionalized genetically engineered spider silk. *Biomaterials* **2011**, *32,* 4255. [CrossRef] [PubMed]

[161 161] Hardy, J. G.; Lea-Egaña, A.; Scheibel, T. R. Engineered Spider Silk Protein-Based Composites for Drug Delivery. *Macromolecular Bioscience* **2013**, *13,* 1431. [CrossRef] [PubMed]

[162 162] Hofer, M.; Winter, G.; Myschik, J. Recombinant spider silk particles for controlled delivery of protein drugs. *Biomaterials* **2012**, *33,* 1554. [CrossRef][PubMed]

[163] Lammel, A.; Schwab, M.; Hofer, M.; Winter, G.; Scheibel, T. Recombinant spider silk particles as drug delivery vehicles. *Biomaterials* **2011**, *32,* 2233. [CrossRef] [PubMed]

[164] Baumann, T.; Kämpfer, U.; Schürch, S.; Schaller, J.; Largiadèr, C.; W. Nentwig, W.; Kuhn-Nentwig, L. Ctenidins: antimicrobial glycine-rich peptides from the hemocytes of the spider *Cupiennius salei. Cellular and Molecular Life Sciences* **2010**, *67,* 2787. [CrossRef] [PubMed]

[165] Vetter, I.; Lewis, R. J. Therapeutic Potential of Cone Snail Venom Peptides (Conopetides). *Current Topics in Medicinal Chemistry* **2012**, *12,* 1546. [CrossRef] [PubMed]

[166] Cheng, S-L.; Lai, Y-L.; Lee, M-C.; Shen, P-C.; Liu, S-S.; Liu, B-T. Effects of deer velvet extract from Formosan sika deer on the embryonic development and anti-oxidative enzymes mRNA expression in mouse embryos. *Journal of Ethnopharmacology* **2014**, *154,* 600. [CrossRef] [PubMed]

[167] Tseng, S-H.; Sung, C-H.; Chen, L-G.; Lai, Y-J.; Chang, W-S.; Sung, H-C.; Wang, C-C. Comparison of chemical composition and osteoprotective effects of different sections of velvet antler. *Journal of Ethnopharmacology* **2014**, *151,* 352. [CrossRef] [PubMed]

[168] Sui, Z. G.; Zhang, L. H.; Huo, Y. S.; Zhang, Y. K. Bioactive components of velvet antlers and their pharmacological properties. *Journal of Pharmaceutical and Biomedical Analysis* **2014**, *87,* 229. [CrossRef] [PubMed]

[169] [169] Wu, F. F; Li, H. Q.; Jin, L. J.; Lin, X. Y.; Ma, Y. S.; You, J. S.; Li, S. Y.; Xu, Y. P. Deer antler base as a traditional Chinese medicine: A review of its traditional uses, chemistry and pharmacology. *Journal of Ethnopharmacology* **2013**, *145,* 403. [CrossRef] [PubMed]

[170] Tseng, S-H.; Sung, H-C.; Chen, L-G.; Lai, Y-J.; Wang, K-T.; Chang, W-S.; Sung, C-H.; Wang, C-C. Effects of Velvet Antler with Blood on Bone in Ovariectomized Rats. *Molecules,* **2012**, *17,* 10574. [CrossRef] [PubMed]

[171] Buthelezi, S.; Southway, C.; Govinden, U.; Bodenstein, J.; Toit, K. An investigation of the antimicrobial and anti-inflammatory activities of crocodile oil. *Journal of Ethnopharmacology* **2012**, *143,* 325. [CrossRef] [PubMed]

[172] Li, H-L.; Chen, L-P.; Hu, Y-H.; Qin, Y.; Liang, G.; Xiong, Y-X.; Chen, Q-X. Crocodile Oil Enhances Cutaneous Burn Wond Healing and Reduces Scar Formation in Rats. *Academic Emergency Med*icine **2012**, *19,* 265. [CrossRef] [PubMed]

[173] Srihongthong, S.; Pakdeesuwan, A.; Daduang, S.; Araki, T.; Dhiravisit, A.; Thammasirirak, S. Complete amino acid sequence of globin chains and biological activity of fragmented crocodile hemoglobin (*Crocodylus siamensis*). *The Protein Journal.* **2012**, *31,* 466. [CrossRef] [PubMed]

[174] Song, W.; Li, S-S.; Qiu, P-P.; Shen, D-Y.; Tian, L.; Zhang, Q-Y.; Liao, L-X.; Chen, Q-X. Apoptosis Induced by Aqueous Extracts of Crocodile Bile in Human Hepatocarcinoma SMMC-7721. *Applied Biochemestry and Biotechnology* **2013**, *170,* 15. [CrossRef] [PubMed]

[175] Kang, J-E.; Zhang, W-Q.; Song, W.; Shen, D-Y.; Li, S-S.; Tian, L.; Shi, Y.; Liang, G.; Xiong, Y-X.; Chen, Q-X. Apoptosis Mechanism of Human Cholangiocarcinoma Cells Induced by Bile Extract from Crocodile. *Applied Biochemistry and Biotechnology* **2012**, *166,* 942. [CrossRef] [PubMed]

[176] Song, W.; Shen, D-Y.; Kang, J-H.; Li, S-S.; Zhan, H-W.; Shi, Y.; Xiong, Y-X.; Liang, G.; Chen, Q-X. Apoptosis of human cholangiocarcinoma cells induced by ESC-3 from *Crocodylus siamensis* bile. *World Journal of Gastroenterology* **2012**, *18,* 704. [CrossRef] [PubMed]

[177] Kommanee, J.; Preecharram, S.; Daduang, S.; Temsiripong, Y.; Dhiravisit, A.; Yamada, Y.; Tharmmasirirsk, S. Antibacterial activity of plasma from crocodile (*Crocodylus siamensis*) against pathogenic bacteria. *Annals of Clinical Microbiology and Antimicrobials* **2012**, *11,* 22. [CrossRef] [PubMed]

[178] Hao, J.; Li, Y-W.; Xie, M-Q.; Li, A-X. Molecular cloning, recombinant expression and antibacterial activity analysis of hepcidin from Sinensis crocodile (*Crocodylus siamensis*). *Comparative Biochememistry and Physiology Part B* **2012**, *163*, 309. [CrossRef]

[179] Jain, C.P.; Dashora, A.; Garg, R.; Kataria, U.; Vashistha, B. Animal self-medication

through natural sources. *Natural Product Radiance* **2008**, *7,* 49. [Link]
[180] Lisonbee, L. D.; Villalba, J. J.; Provenza, F. D.; Hall, J. O. Tannins and self-medication: Implications for sustainable control in herbivores. *Behavioral Process,* **2009**, *82,* 184. [CrossRef] [PubMed]
[181] Villalba, J. J.; Landau, S. Y. Host behavior, environment and ability to self-medicate. *Small Ruminant Research* **2012**, *103,* 50. [CrossRef]
[182] Fruth, B.; Ikombe, N. B.; Matshimba, G. K.; Metzeger, S.; Muganza, D. M.; Mundry, R.; Fowler, A. New Evidence for Self-Medication in Bonobos: *Manniophyton fulvum* Leaf- and Semstrip-Swallowing from LuiKotale, Salonga National Park, DR Congo. *American Journal of Primatology* **2014**, *76,* 146. [CrossRef] [PubMed]
[183] Menzel, C.; Fowler, A.; Tennie, C.; Call, J. Leaf Surface Roughness Elicits Leaf Swallowing Behavior in Captive Chimpanzees (*Pan troglodytes*) and Bonobos (*P. paniscus*), but not in Gorillas (*Gorilla gorilla*) or Orangutans (*Pongo abelii*). *International Journal of Primatology* **2013**, *34,* 533. [CrossRef]
[184] Masi, S.; Asselain, N.; Robelin, L.; Bourgeois, A.; Hano, C.; Dousseau, G.; Jalme, M. S.; Krief, S. Response to bitter substances in primates: Roles of diet tendency and weaning age. *Cognitive Affective & Behavioral Neuroscience* **2013**, *13,* 916. [CrossRef] [PubMed]
[185] Chaves, O. M.; Bicca-Marques, J. C. Dietary Flexibility of the Brown Howler Monkey Throughout Its Geographic Distribution. *American Journal of Primatology* **2013**, *75,* 16. [CrossRef] [PubMed]
[186] Pascual-Garrido, A.; Buba, U.; Nozda, G.; Sommer, V. Obtaining raw material: plants as tool sources for Nigerian chimpanzees. *Folia Primatologica* **2012**, *83,* 24. [CrossRef] [PubMed]
[187] Norscia, I.; Ramanamanjato, J. P.; Ganzhorn, J. U. Feeding Patterns and Dietary Profile of Nocturnal Southern Wooly Lemurs (*Avahi meridionalis*) in Southeast Madagascar. *International Journal of Primatology* **2012**, *33,* 150. [CrossRef]
[188] McLennan, M. R.; Huffman, M. A. High Frequency of Leaf Swallowing and Its Relationship to Intestinal Parasite Expulsion in "Village" Chimpanzees at Bulindi, Uganda. *American Journal of Primatology* **2012**, *74,* 642. [CrossRef] [PubMed]
[189] Masi, S.; Gustafsson, E.; Jalme, M. S.; Narat, V.; Todd, A.; Bomsel, M-C.; Krief, S. Unusual feeding behavior in wild great apes, a window to understand origins of self-medication in humans: Role of socially and physiology on learning process. *Physiology & Behavior* **2012**, *105,* 337. [CrossRef]
[190] Alfaro, J. W. L.; Matthews, L.; Boyette, A. H.; MacFarland, S. J.; Phillips, K. A.; Falotico, T.; Ottoni, E.; Verderane, M.; Izar, P.; Schulte, M.; Melin, A.; Fedigan, L.; Janson, C.; Alfaro, M. E. Anointing Variation Across Wild Capuchin Populations: A Review of Material Preferences, Bout Frequency and Anointing Socially in *Cebus* and *Sapajus. American Journal of Primatology* **2012**, *74,* 299. [CrossRef]
[191] Gustafsson, E.; Krief, S.; Jalme, M. S. Neophobia and Leraning Mechanisms: How Captive Orangutans Discover Medicinal Plants. *Folia Primatologica* **2010**, *82,* 45. [CrossRef] [PubMed]
[192] Marques, V.R.B. *Natureza em boiões: Medicina e boticários no Brasil setecentisata.* Editora da UNICAMP. Campinas, **1999**.
[193] Medeiros, M. F.; Albuquerque, U.P. Food flora in 17th century northeast region of Brazil in *Historia Naturalis Brasiliae. Journal of Ethnobiology and Ethnomedicine* **2014**, *10,* 50. [CrossRef] [PubMed]
[194] Breitbach, U. B.; Niehues M.; Lopes, N. P.; Faria, J. E. Q.; Brandão, M. G. L. Amazonian Brazilian medicinal plants described by C. F. M. von Martius in the 19th century. *Journal of Ethnopharmacology* **2013**, *147,* 180. [CrossRef] [PubMed]
[195] Sá, I. M.; Elisabetsky, E. Medical knowledge exchanges between Brazil and Portugal: An ethnopharmacological perspective. *Journal of Ethnopharmacology* **2012**, *142,* 762. [CrossRef] [PubMed]
[196] Medeiros, M. F. T.; Albuquerque, U. P. The pharmacy of the Benedictine monks: The use of medicinal plants in Northeast Brazil during the nineteenth century (1823-1829). *Journal*

of Ethnopharmacology **2012**, *139,* 280. [CrossRef] [PubMed]
[197] Giorgetti, M.; Negri, G. Plants from Solanaceae family with possible anxiolytic effect reported on 19th century's Brazilian medicinal journal. *Brazilian Journal of Pharmacognosy* **2011**, *21,* 772. [CrossRef]
[198] Brandão, M. G. L.; Pignal, M.; Romaniuc, S.; Grael, C. F. F.; Fagg, C. W. Useful Brazilian plants listed in the field books of the French naturalist August de Saint-Hilaire (1779-1853). *Journal of Ethnopharmacology* **2012**, *143*, 488. [CrossRef][PubMed]
[199] CNPq. Conselho Nacional de Desenvolvimento Científico e Tecnológico. www.cnpq.org.br. Accessed on March 12, **2014**.
[200] Calixto, J. B. Twenty-five years of research on medicinal plants in Latin America. *Journal of Ethnopharmacology* **2005***, 100,* 131. [CrossRef] [PubMed]
[201] Albuquerque, U. P.; Silva, J. S.; Campos, J. L. A.; Sousa, R. S.; Silva, T. C.; Alves, R. R. N. The current status of ethnobiological research in Latin America: gaps and perspectives. *Journal of Ethnobiology and Ethnomedicine* **2013**, *9,* 72. [CrossRef] [PubMed]
[202] Human Development Report. The Rise of the South. Human Progress in a Diverse World. The United Nations Development Programme, New York, **2013**.