PERGAMON

Phytochemistry 60 (2002) 145–152

PHYTOCHEMISTRY

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Integration of ethnobotany and phytochemistry: dream or reality?

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Received in revised form 21 December 2001

Abstract

The major challenge of this paper comprises an attempt to compare the wealth of folk-information based on "traditional knowledge" with the efficacy of a chemo-biological background based on scientific knowledge. Surprisingly, correlations between plant uses (as food and medicine) and evolutionary status according to morphology (as assigned by Sporne indices) and metabolism (as assigned by diversity of phytochemicals) obey strikingly uniform systematic and evolutionary trends. The resulting patterns suggest a dynamic chemical mechanism for the bioactivity in plants regulated by the antagonistic gallate/caffeate pair. This finding is an important step toward the construction of a coherent chemo-biological language by a dynamic holistic quantitative methodology, one of the most potent prospects for understanding the functioning of nature. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Ethnobotany; Angiosperms; Medicinal species; Edible species; Antagonisms; Gallic acid; Caffeic acid

1. Introduction

"The question for the new millennium is whether, when we have never been better poised technologically to evaluate natural products, these advances will occur fast enough to overtake the current rates of plant extinction and indigenous culture loss. Will tribal knowledge survive this millennium? If it doesn't, the world will be far poorer for its loss" (Cox, 2000).

Although much effort could be saved by tapping the experience and wisdom of traditional healers, it is our understanding that only science will reveal the full potentialities of medicinal plants. Indeed, should traditional practices be explainable by modern science-oriented concepts, predictions concerning the natural distribution of plant products endowed with desired biological properties could be investigated speedily and routinely, free from the tedious effort employed in the demystification of popular beliefs (Gottlieb, 1982).

At this point, we anticipate the impact of the traditional healer *vs.* the modern physician, by searching patterns of similarity between these apparently different types of knowledge. Only a coherent language can achieve the integration of structural (chemical) and functional (biological) terms capable of constructing a model used as a guide for the comparison of the properties of organisms. After all, the biological functions of plants are also due to their diverse chemical arsenal. Thus, our major challenge consists in the replacement of the traditional, i.e. static–reductive–narrative approach, by a dynamic–holistic–quantitative methodology, potentially one of the prospects for understanding of the functioning of nature.

2. Ethnobotanical background

In a previous attempt to validate Amazonian ethnobotany by patterns of plant evolution we chose appropriate databases. The first group listed plants utilized by three indigenous societies living in different parts of Amazonia, particularly Chácobo (Bolívia) (Boom, 1989), Kayapó (Pará, Brazil) (Anderson and Posey, 1989), and Ka'apor (Maranhão, Brazil) (Balée and Gély, 1989). The second group listed plants utilized by three nonhuman primates: cebuella (Amazonia) (Soini, 1988), spider

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PII: S0031-9422(02)00088-2

monkey (Pará and Guiana) (Roosmalen and van Kecin, 1988), and muriqui (Atlantic forest) (Nishimura et al., 1988; Strier, 1991).

In both groups the correlation between the frequency of useful plants with an evolutionary parameter based on herbaceousness indices for superorders revealed a common trend: more primitive plant species are used as foods, and more recently evolved plant species are selected as medicines (Gottlieb and Borin, 1997; Gottlieb et al., 1995a, 1996a).

In an attempt to verify the generality of the previous results, a major database extracted from a significantly vast ethnobotanical survey (Pio Corrêa, 1984) was selected. This inventory was elaborated during the first years of the 20th century, chiefly in Brazil, prior to the more recent, massive deforestations of South America. The encouraging results confirmed the systematic and evolutionary patterns previously determined for food and medicine species, and enhanced the understanding of the chemical mechanisms regulating the production of bioactive products (Gottlieb et al., 2001).

3. Methods

3.1. Databases

To further substantiate the universality of the previous results, ethnobotanical inventories, representative of different regions and continents, were selected. Besides the three regionally and ethnically restricted inventories (Chácobo, Kayapó, and Ka'apor) and the extensive Brazilian ethnobotanical survey (Pio Corrêa), four lists of useful plants from Amazonia (three from Brazilian Amazonia, and one from Peruvian Amazonia), two from North America, and two from Africa (Table 1) were selected.

3.2. Ethnobotanical parameters—qualitative models

From each inventory, the dicotyledon species, to which useful (e.g. edible, medicinal) properties had been assigned by popular recommendation, were catalogued and listed in their respective families. They were arranged according to Dahlgren's system of classification: a diagram showing the angiosperm orders as "bubbles" in which the relative numbers of species involved are indicated by size of the figures. Their relative positions approximated to the mutual similarity of attributes reflect phylogenetical affinity (Dahlgren, 1980). Other morphological arrangements of angiosperms should also fulfill the purpose of this paper.

Dicotyledon orders, assigned by ethnobotanical information as foods and medicines, etc. were indicated in this dahlgrenogram by different colors to illustrate the preponderant uses of their species. For example, Pio Corrêa's survey listed for the order Laurales (superorder Magnoliiflorae) 8 food species, 26 medicinal species, and 1 toxic species. Hence, the predominance of medicinal species in this order was indicated by the pink color in the dahlgrenogram (Fig. 1).

3.3. Evolutionary parameter

The species listed in each ethnobotanical inventory were classified in the respective dicotyledon families, characterized by evolutionary status according to Sporne indices (*SI*). This evolutionary parameter indicates how infrequent is the presence of 30 chiefly morphologic characters regarded as "primitive", in each of 291 dicotyledon families (Sporne, 1980). The means of *SI* of the pertinent, useful families were attributed to the evolutionary status of the respective orders. For example, Pio Corrêa's survey listed useful species for Monimiaceae (*SI* = 47) and Lauraceae (*SI* = 52) of the order

Table 1
Number of useful dicotyledon species registered in different ethnobotanical inventories

Ethnobotanical inventories	Codes	Number of dicotyledon species cited as				Total of species	
		Foods	Medicines	Nutraceuticals	Poisons		
Africa	Af-1	1538				1538	Peters et al., 1992
Africa	Af-2		924			924	Iwu, 1993
North America	NAm-1	841				841	Beckstrom-Sternberg and Duke, 1994
North America	NAm-2		2050			2050	Beckstrom-Sternberg et al., 1995
Brazil	Br-1	458	841	92	236	1627	Pio Corrêa, 1984
Brazil-Amazonia	Br-2	137				137	Cavalcante, 1996
Brazil-Amazonia	Br-3		52			52	Stasi et al., 1989
Brazil-Amazonia	Br-4		296			296	Matta, 1913
Peru-Amazonia	Pe-1		56			56	Desmarchelier and Schaus, 2000
Chácobo	Cha	59	109	23	5	196	Boom, 1989
Kayapó	Kay	12	63	17		92	Anderson and Posey, 1989
Ka'apor	Kaa	38	22	7		67	Balée and Gély, 1989

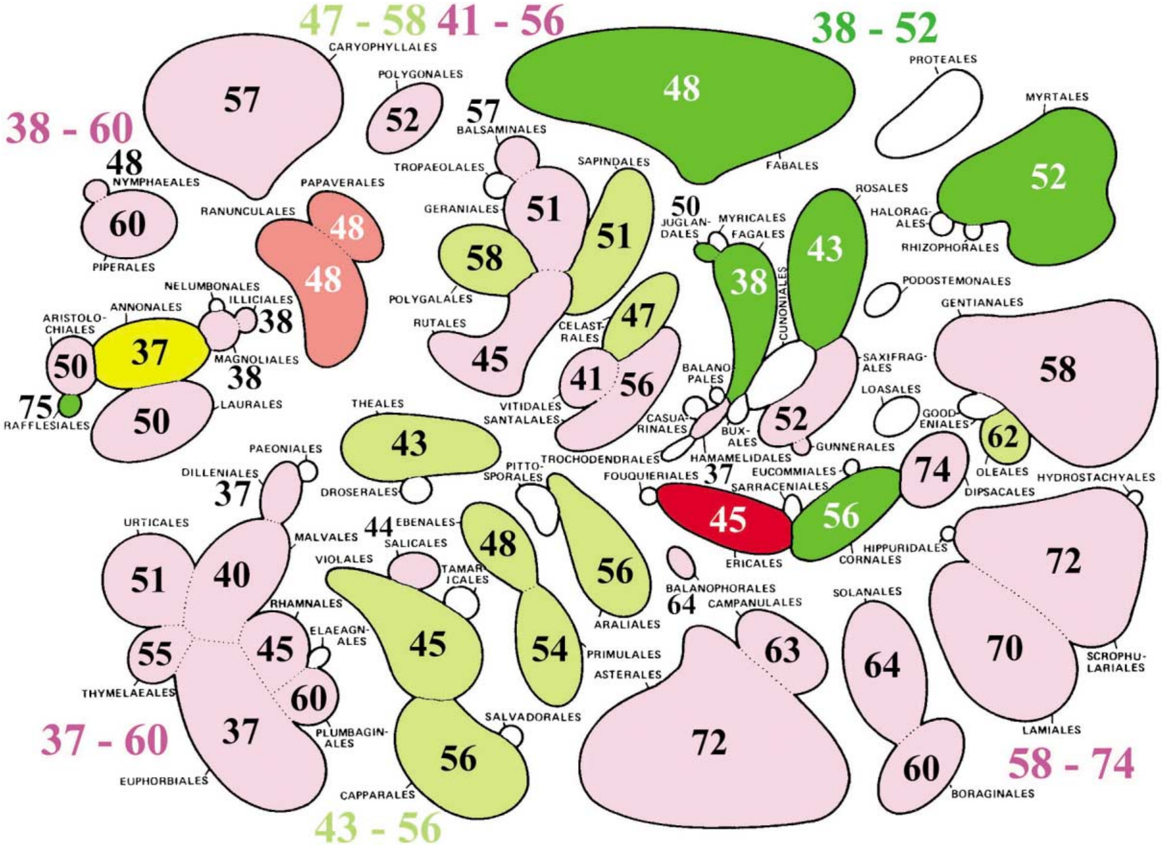

Fig. 1. A dahlgrenogram (Dahlgren, 1980) for dicotyledons, illustrating preferential uses of species in orders, represented by ‘‘bubbles’’, as medicines (pink), foods (dark green), nutraceutics (yellow), poisons (dark red), poisons and medicines (light red), and medicines and foods (light green) based on Pio Corrêa’s survey (1984). The orders were characterized by an evolutionary parameter [Sporne indices (1980)] obtained by the means of *SI* of the pertinent useful families.

Laurales (superorder Magnoliiflorae). Thus, the mean value $SI = 50$ was attributed to this order (Fig. 1).

3.4. *Ethnobotanical parameters—quantitative models*

With the aim of quantifying the evolutionary trends for the ethnobotanical patterns, the dicotyledon families were classified according to their evolutionary status given by Sporne indices (see Section 3.3). In this procedure, the families are arranged in evolutionary groups (according to *SI* values) and not in the usual way, i.e. in systematical groups (in orders and superorders according to Dahlgren’s classificatory system).

The construction of the quantitative ethnobotanical models (‘‘spectra’’) lead to the determination of evolutionary patterns for each type of bioactivity. For example, in Pio Corrêa’s survey the dicotyledon families characterized by $SI = 52$ (Lauraceae, Polygonaceae, Capparidaceae and Anacardiaceae) add up to 16 food species (8, 1, 1, and 6 food species, respectively). Thus, in this ethnobotanical inventory, families with $SI = 52$ include 3.5% of the food species (16 food species in the total of 458 food species) (indicated by an arrow in Fig. 2). Hence, each Sporne index value (*SI*) can be characterized by a percentage of food and medicinal species of an ethnobotanical inventory (Fig. 2).

3.5. *Chemical parameters—quantitative models*

Diversification of micromolecular categories in plant groups are represented by frequencies [numbers of occurrences (NO)]. The NO of a selected biosynthetic category, known to occur in a family, is established by the total number of compounds registered for all their species. Hence, if a compound is registered for ‘‘*n*’’ different species it is counted ‘‘*n*’’ times.

The construction of the quantitative evolutionary models was also performed according to the method described above (see Section 3.4). However, in the present case the percentages of useful species (ethnobotanical information) are replaced by percentages of micromolecular occurrences (chemical information) based on distribution of compounds previously determined for angiosperm families (Gottlieb et al., 1995b, 1996b). Thus, each Sporne index value (*SI*), was characterized by the percentage of diversification of a micromolecular category (NO%) (Fig. 3). For example, the dicotyledon families characterized by $SI = 52$ (Lauraceae, Urticaceae,

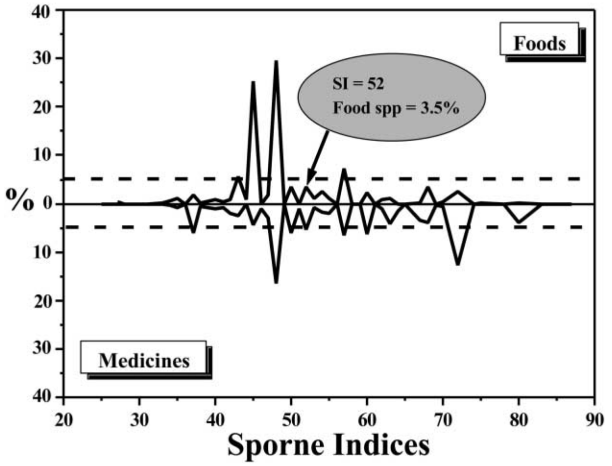

Fig. 2. Evolutionary spectrum indicating, for each evolutionary status [described by *SI* (Sporne, 1980)], the number of species (in percentage values) qualified as foods (full lines in the top part of the "spectra") and as medicines (full lines in the bottom part of the "spectra") in an ethnobotanical survey (Pio Corrêa, 1984). Normalization was effected considering the total number of species cited for each ethnobotanical application (foods and medicines). The dashed lines correspond to 5% of food and medicinal species. The peak indicated by an arrow refers to an example cited in the text (see Section 3.4).

Aceraceae, Anacardiaceae, Sambucaceae, Ulmaceae, and Polygonaceae) add up to 57 caffeate occurrences [NO(CAF) = 5, 1, 1, 4, 4, 10, and 32, respectively]. Thus, families with *SI* = 52 include 4.5% of the caffeate occurrences (57 occurrences in the total of 1255 caffeate occurrences in dicotyledon families) (indicated by an arrow in Fig. 3C).

In contrast to the static traditional and qualitative botanical classifications, this dynamic quantitative evolutionary system can be applied to characters of multiple nature (morphological, geographical, ethnobotanical, or chemical), allowing comparisons among them.

4. Results

4.1. Ethnobotany and systematic observations

The trends among the qualifications of angiosperm species must possess systematic relevance in order to promote ethnobotanical descriptions to valid quantitative evolutionary parameters. Indeed, juxtaposing ethnobotanical data, listed in the major survey (Pio Corrêa, 1984), with evolutionary data (*SI*) on a dahlgrenogram shows extraordinary consistencies (Fig. 1). The same preferential use, indicated by identical colors, is observed for the different orders of major superorders. These similarities become more obvious in two cases: for medicinal plants in the relatively advanced orders (*SI* = 58–74) displayed at the right bottom corner of the diagram (Asteridae *sensu* Cronquist, 1988), and for food plants in the relatively more primitive orders (*SI* = 38–

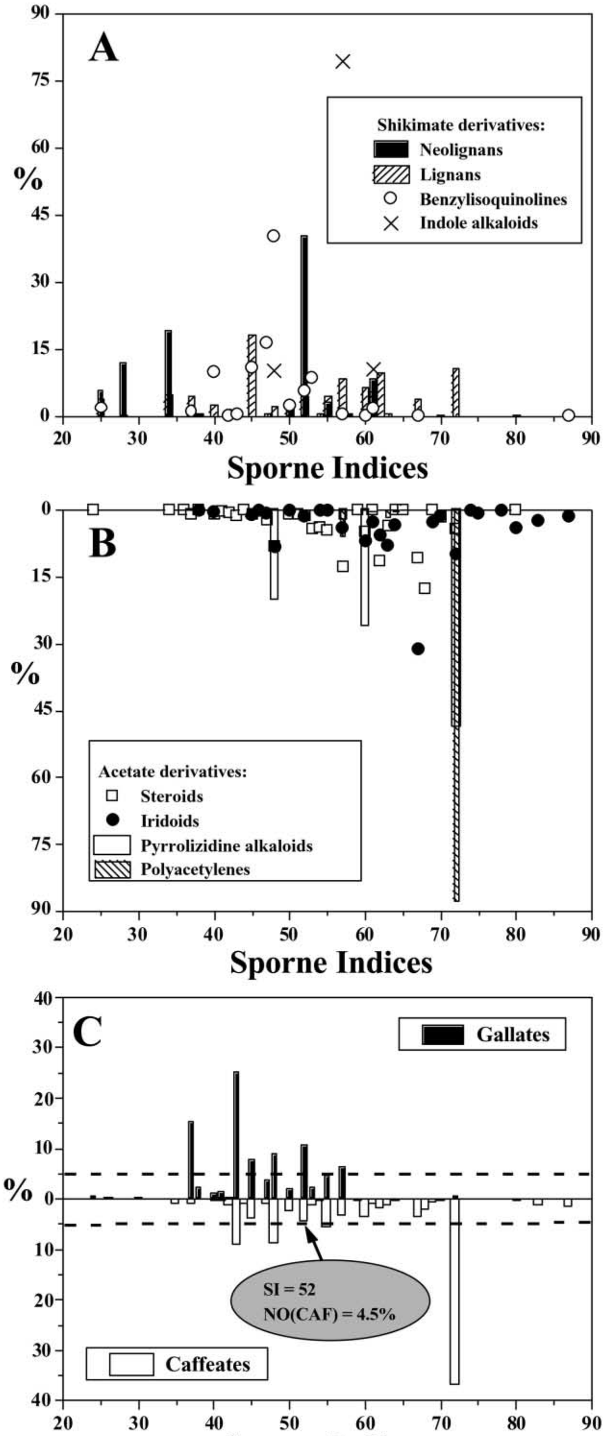

Fig. 3. Number of occurrences, in percentage values, of selected micromolecular categories (each normalized to 100%) of chemically better known dicotyledon families arranged according to their evolutionary status [morphological advancement indices, Sporne indices (1980)]. A: shikimate derivatives. Indole alkaloids, originated by both biosynthetic pathways (mixed biosynthesis), were plotted jointly with shikimate because they represent one of the last evolutionary steps of diversification of this pathway; B: acetate derivatives; C: gallate (top) and caffeate (bottom) derivatives. The dashed lines correspond to 5% of gallates and caffeates. The peak indicated by an arrow refers to an example cited in the text (see Section 3.5). For database see Gottlieb et al., 1995b, 1996b.

52) displayed at the right top corner of the diagram (Fig. 1). In addition, preference for plants used as foods characterizes two clusters appearing at more internal locations displayed at the diagonal from bottom left to top right (the Hamamelidae–Dilleniidae–Rosidae complex *sensu* Cronquist).

Some cases may at first sight seem discordant when examined in greater detail; e.g. the orders of the superorder Rutiflorae are preferentially medicinal, with the exception of Sapindales and Polygalales which are used as medicine, as well as food. Surprisingly, the former order is considered to be strongly related to the order Fabales (preferentially used as food), being inclusively united in a more recent edition of the diagram (Dahlgren, 1995). Thus, probably Sapindales form a link between a medicinal group and one of the edible clusters. Identical discussion can be promoted for the order Celastrales, with the same proportion of medicinal and food species, also included recently in the superorder Rutanae (ex Rutiflorae).

All data on plant uses are based on the traditional interviews, and hence their consistence with the distribution of superorders in Dahlgren's scheme is truly astounding. An analogous close consistence of ethnobotanical data and Cronquist's classificatory scheme for angiosperms (Cronquist, 1988), even if limited to incomparably smaller populations of human (Gottlieb et al., 1995a) and non-human South American primates (Gottlieb et al., 1996a) has been published.

The present state of the work shows two phenomena to characterize evolution in both directions: gradual replacement of food plants first by medicinal plants toward poisonous plants; and gradual passage from ethnobotanically heterogeneous clusters into homogeneous clusters, suggested by the unification of colors, and the increase of percentage values of medicinal species per taxon in Asteridae (Fig. 1).

4.2. Ethnobotany and evolutionary observations

Construction of quantitative evolutionary models based on ethnobotanical information (see Section 3.4), allowed determination of evolutionary patterns for each type of bioactivity (Fig. 2). Even though each ethnobotanical inventory shows different particularities, due chiefly to different local circumstances, a global analysis may reveal similar patterns.

In order to compare the several different databases, we have marked the major peaks (above the dashed lines in Fig. 2), i.e. above 5% of food and medicinal species for each inventory (Fig. 4). For instance, $SI = 45$, 48, and 57 correspond to maxima for food plants everywhere. However, $SI = 37$, 48, 57, and 72 correspond to maxima for medicine plants in nearly all inventories. Hence in general, food species are limited by intermediate evolutionary status ($SI = 45$–57), only rarely attaining higher or lower SI values. Exceptions ($SI = 72$) for Africa may indicate lack of foods; and for North America, where species utilized as beverage and other stimulants are considered additional food plants. In opposition, medicinal species occupy a large *SI* range ($SI = 37$–72), often present at high evolutionary status ($SI = 72$, 80). An uncertain situation occurs with families of intermediate status, where we find a quasi equilibrium between types of useful plants (Fig. 4).

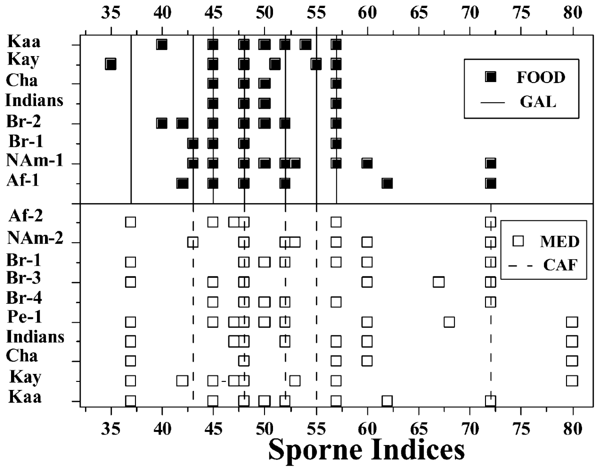

Fig. 4. Sporne indices of the more intense peaks, i.e. above 5% of food (dark squares) and medicinal (light squares) species for different ethnobotanical inventories. For example, the values to Br-1 [Pio Corrêa's survey (1984)] correspond to the peaks situated above dashed lines in Fig. 2. The vertical lines indicate the major peaks, i.e. above 5% (peaks situated above dashed lines in Fig. 3C), of occurrences of gallates (full lines) and caffeates (dashed lines). For legend to inventory codes see Table 1. "Indians" refer to the inventory of the three Amazonian indigenous societies (Chácobo, Kayapó and Ka'apor) considered together.

5. Discussion

5.1. Chemical background

We have previously reported the correlation of phytochemicals with *SI* (Gottlieb and Borin, 1998a, b). To mention only the major central machinery, evolution of compounds within shikimate and acetate-derived metabolic categories obeys identical kinetics: the diversity of compounds (indicated by NO) increases gradually with evolution (indicated by *SI*). This induction of diversification is followed by a maximum prior to fast decrease and substitution of one category by another one, but not by clear-cut exclusions (Fig. 3A and B).

Thus, first neolignans are replaced by benzylisoquinolines, second benzylisoquinolines are replaced by anthranilate-derived alkaloids and indole alkaloids, and third indole alkaloids are replaced by steroids, iridoids, polyacetylenes and pyrrolizidine alkaloids. Indole alkaloids, originating from two (anthranilate and iridoid moieties) biosynthetic pathways, represent one important step in this evolutionary substitution of shikimate by acetate derivatives. Thus, upon evolution (SI 57→61) production of complex indoles decreases (NO 79.3%→ 10.5%) (Fig. 3A), whereas concomitantly (*SI* 57→67) production of simple iridoids increases (NO 4.1%→ 31.2%) (Fig. 3B).

Gallate is rare in the Magnoliidae of low *SI*, frequent in the Hamamelidae–Dilleniidae–Rosidae complex, of intermediate *SI*, but antagonized by caffeate, and does not occur in Asteridae of high *SI* (Fig. 3C). Thus, the identity, structure and function of phytochemicals obey evolutionary trends and can be integrated.

This type of analysis allows the observation of many important points: in TIME, "evolutionary substitutions" occur between both metabolic pathways (shikimate and acetate) as well as among different metabolic categories (for instance neolignans and benzylisoquinolines); in SPACE, "ecological complementations" allow at the same evolutionary status the co-occurrence of both metabolic pathways, the shikimate/acetate routes, as well as of many metabolic categories; a sudden decrease of all metabolic categories occurs at the *SI*-range between 35 and 45. It is precisely at this evolutionary status that great diversification of gallates takes place; great diversity of metabolic categories occurs also at high evolutionary status, *SI* = 72, characteristic of caffeates.

5.2. *Bioactivity mechanisms*

At first sight, the quantitative evolutionary models based on GAL- and CAF-information, demonstrated very different features with two complementary parts (Fig. 3C). It is easy to distinguish a central part with about equally balanced GAL/CAF portions, flanked by much more intense and practically unbalanced GAL and CAF terminals situated, respectively, at the low and the high *SI* terminals. This immediately suggests the dualistic nature of the model, a neat antagonistic pattern, possibly a valuable model for bioactive compounds.

Considering that the biological activity of plants is the consequence of their chemical composition, the apparently complementary nature of food and medicine species requires rationalization by a metabolic regulatory mechanism. Hence, the selection of gallates (GAL) and caffeates (CAF) for this purpose is realistic for two reasons: (1). both are regulators of intermediate metabolism in consequence of their respective negative and positive feedback action (Boudet et al., 1971; Gottlieb and Borin, 1998b, 2000); (2) both possess systematically significant distribution in angiosperms (Gottlieb and Borin, 1998b, 2000; Gottlieb et al., 1995b).

Comparison of the quantitative model based on ethnobotany with the universal phytochemical background, suggest a chemical mechanism for bioactivity (Fig. 5). Indeed, the "spectral" features of the GAL-model are similar to the ethnobotany-guided food plants. In contradistinction, the analogous features of the CAF-model are similar to the ethnobotany-guided medicine plants (Fig. 5).

Again in order to compare several different databases, we have marked the major GAL/CAF peaks (above the dashed lines in Fig. 3C), i. e. above 5% for each inventory (vertical lines in Fig. 4). Therefore, the three maxima of food plants for practically all inventories correspond to *SI* = 45, 48 and 57. At these exact positions there are maxima for GAL. Analogously, at *SI* = 72 there is a maximum for medicine plants and CAF.

Statistical validation of the degree of association between the two quantitative models, ethnobotany and phytochemistry, was obtained via coefficients of linear regression (r). Thus, we correlated the distribution of food species for each ethnobotanical inventory with the diversity of gallates (GAL) and caffeates (CAF), both determined for each evolutionary status according to the Sporne indices (*SI*) (Table 2). At first sight, analysis of the coefficients of linear regression (r) for food species would suggest only a small degree of association with gallate diversification (GAL). However, we should observe two important points: first, the coefficient values are nearly always higher with gallates than caffeates; second, plants with higher concentration of GAL, at *SI* = 37 and 43, lose their nutritional value. For this reason, these plants are not useful as food. However, in sequence (at *SI* = 45) the antagonistic effect of caffeate diminishes the diversity of GAL, decreasing the astringency and allowing the utilization of these plants as food. This occurs because in spite of this decrease in astringency, the GAL concentration is still sufficiently high to cause the inhibitory effect on micromolecular diversity (Gottlieb and Borin, 1998b, 2000; Gottlieb et al., 1995b), and hence, toxicity remains.

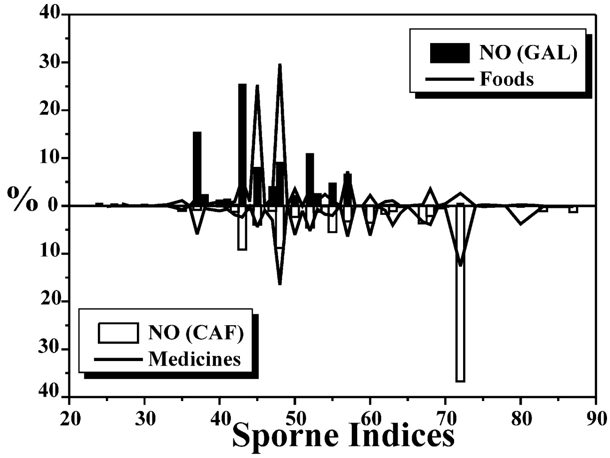

Fig. 5. Superposition of evolutionary spectra based on ethnobotanical (Pio Corrêa, 1984) (Fig. 2) and phytochemical (Gottlieb et al., 1995b, 1996b) (Fig. 3C) data. Top: Number of species used as foods (full lines) and number of occurrences of gallates (dark bars). Bottom: Number of species used as medicines (full lines) and number of occurrences of caffeates (light bars).

Table 2
Coefficients of linear regression (*r*) for correlations among occurrence of gallates [NO(GAL)] and caffeates [NO(CAF)] and number of food and medicinal species in dicotyledon families in different ethnobotanical inventories

Codes[a]	Foods		Medicines	
	NO (GAL)	NO (CAF)	NO (GAL)	NO (CAF)
Af-1	0.337 ($P=0.0361$)	0.379 ($P=0.0159$)		
Af-2			0.395 ($P=0.0106$)	0.541 ($P=0.0002$)
NAm-1	0.567 ($P=0.0006$)	0.720 ($P<0.0001$)		
NAm-2			0.357 ($P=0.0186$)	0.933 ($P<0.0001$)
Br-1	0.421 ($P=0.0086$)	0.242 ($P=0.1322$)	0.361 ($P=0.0203$)	0.660 ($P<0.0001$)
Br-2	0.296 ($P=0.0797$)	0.128 ($P=0.4510$)		
Br-3			0.200 ($P=0.2431$)	0.755 ($P<0.0001$)
Br-4			0.348 ($P=0.0299$)	0.338 ($P=0.0332$)
Pe-1			0.355 ($P=0.0312$)	0.172 ($P=0.3033$)
Indians[b]	0.298 ($P=0.1091$)	0.145 ($P=0.3864$)	0.344 ($P=0.0343$)	0.204 ($P=0.2203$)
Cha	0.325 ($P=0.0496$)	0.148 ($P=0.3803$)	0.270 ($P=0.1062$)	0.142 ($P=0.3958$)
Kay	0.226 ($P=0.1852$)	0.114 ($P=0.5080$)	0.304 ($P=0.0712$)	0.198 ($P=0.2401$)
Kaa	0.295 ($P=0.1142$)	0.118 ($P=0.4846$)	0.484 ($P=0.0032$)	0.236 ($P=0.1649$)

[a] For legends and refs. see Table 1.
[b] Inventories of the three Amazonian indigenous societies (Chácobo, Kayapó and Ka'apor) considered together.

Additionally, for each ethnobotanical inventory the correlations between distribution of medicinal species with diversity of gallates (GAL) and caffeates (CAF) was performed. In analogy with the previous correlations, both variables were determined for each evolutionary status according to Sporne indices (Table 2). Analysis of the coefficients of linear regression (r) for medicinal species of nearly all inventories suggests a stronger degree of association with caffeates than with gallates. Obviously, the closest correlations were obtained for the most extensive (Br-1) and most modern (NAm-2 and Br-3) floristic inventories. Relatively modest inventories (Cha, Kay, Kaa), restricted for limitations of territory can also be obscured by mysticism. The results prove once more the complementary nature of the antagonistic GAL/CAF-model and food/medicine-plants.

6. Conclusion

"Our economy is often referred to as a knowledge-based economy. The increased use that is made of the patent system indicates that a large part of knowledge and technology is being privatized" (van Wijk, 2000). The actual situation has generated an unprecedented dispute among the more diverse levels of our society, as for example consumers, environmentalists, scientists, traditional societies, governments, politicians, economists, business managers, and pharmaceutical companies. To the next generations remain the consequences, good or bad, of the actual ecologic-socio-economic conflicts. Hence, the major challenge for our generation is trying to conciliate antagonistic intents, the economic interests and the well-being of humanity and of planet Earth. Dream or reality?

Parallel with these disputes generated by "phytobusiness", our battle for survival continues. Human health care requires the ever increasing resistance of pathogens to be confronted by a correspondingly fast rate of discovery of novel antibiotics. One of the possible strategies towards this objective involves the rational localization of bioactive phytochemicals. An immediate consequence would be the possibility to alleviate the heavy burden of random selection of plant samples, and consequently to enhance the rate of discoveries of natural products. This task will continue only a distant dream unless the mechanisms responsible for plant bioactivity may be recognized. However, surprisingly little is known about the relationships of natural products with morphology, ecology and evolution of their plant source.

The conceptual basis of our method consists in the incorporation of ethnobotanical codes, expressing biological functions, into a quantitative chemo-biological language. The results demonstrated that traditional knowledge, when considered from a scientific point of view and by an adequate methodology, possesses systematic and evolutionary relevance. This procedure is shown to be a powerful tool to clarify evolutionary mechanisms that regulate bioactivity. Hopefully, it constitutes a new clue for introspection into the general mechanisms of the functioning of nature.

Additionally, the complementary nature of medicine and food species, demonstrated in this paper, can be rationalized by the involvement of plant metabolic cycles regulated via gallate/caffeate feedback loops. Hence, both dualistic systems (medicine/food and GAL/CAF), jointly with a wide range of physical, chemical, biological and social systems, constitute one more, very important example of the universality of antagonistic forces (Gottlieb and Borin, 1998b, 1999), offering the ecological plasticity indispensable for adaptations to environmental changes.

The last, but not less interesting observation is that the number of species reported as medicines is indeed much higher than the number of species reported as foods (Table 1; the predominance of pink color in Fig. 1). Furthermore, the great majority of the dicotyledon families possess medicinal properties in contradistinction with the very few edible ones. Interpreted in a dynamic framework, these facts illustrate the evolutionary replacement of phytochemicals in the direction of gradually more potent vehicles of plant defence against mammals. Thus from the utilitarian point of view, natural products, contrary to our selfish visions, diversify not for us but against us.

Acknowledgements

Supported by a grant from Academia Brasileira de Ciências, Rio de Janeiro, and by fellowships from the Conselho Nacional de Desenvolvimento Científico e Tecnológico, Brasília and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro, Rio de Janeiro, Brazil.

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