arrhythmia, as well as cluster headaches (Hollman, 2005). The anti-asthmatic agent cromolyn (used as sodium cromoglycate) and the antiarrhythmic agent amiodarone were developed from khellin, an extract from the fruits of khella or toothpickweed *Ammi visnaga* (L.) Lam. (Apiaceae; Meyer, 2002; Fitzgerald, 2004). Khellin itself was used in Ancient Egypt to facilitate the discharge of kidney and gallstones, to alleviate the pain of angina pectoris, and as a bronchodilator, but was discontinued for such uses in the USA because of the occurrence of nausea and vomiting after prolonged use.

## THE MARKET

The estimated size of the global market for plant-derived medicinal substances is astonishing, comprising more than 30% of the worldwide sales of drugs (Patwardhan et al., 2004). Expenditures have grown rapidly, from US$ 18 billion in 1,997 to US$ 80 billion in 2,004 (Mathur, 2003; WHO, 2002, 2003), and are expected to reach US$ 5 trillion by the year 2,050 (WHO, 2003).

Asia dominates the world market at about 40% share, with China and India probably representing the largest consumers, producers, and exporters of plant-based medicines. In China, more than 11,000 of the approximately 12,000 plant species are used for traditional medicinal purposes by almost 90% of the population (WHO, 2002, 2003), and these substances comprise about 40% of the medicine consumption in the country (WHO, 2002, 2003). Notably, the total production of herbal medicines in 2001/2002 was approximately 8.8 million tons with a value of approximately US$ 2 billion (Wang and Ren, 2002). In India, about 40% of the roughly 20,000 plant species are used for medicinal purposes, ranking the country first in the world with respect to percent flora which contains active medicinal ingredients (WHO, 2002, 2003). India supplies 12% of the world's requirements of medicinal plants - per year more than 8,000 tons of crude drugs - which earns the country revenues of approximately US$ 50 million per year (Ramakrishnappa, 2002; WHO, 2002, 2003).

The Member States of the European Union and North America hold about 35 and 17% of global shares of plant-derived products, respectively, and rank second and third, respectively, on the list of the largest consumers and producers of plant-derived products (WHO, 2002, 2003). Together with Germany, the USA occupies the top position in the world with respect to the import of raw medicinal plant materials and the export of herbal products in the form of medicines, nutraceuticals, dermaceuticals, fortified foods, and dietary supplements (WHO, 2002, 2003). Notably, in 2004, over 60% of the German population spent US$ 2.2 billion annually on plant-derived medicines (WHO, 2002, 2003), and three out of ten Americans used botanical products at expenditures of over US$ 14 billion per year (De Smet, 2002; WHO, 2002, 2003; Patwardhan et al., 2004; Khalsa, 2006.

Africa, South America, Central America, and the Caribbean provide a considerable part of the raw materials for the products mentioned earlier (WHO, 2002, 2003). Africa harbors more than 4,000 medicinal plant species, and harvests annually more than 50,000 tons of plant material with a value in the billions of US dollars (WHO, 2002, 2003). This includes, among others, the bark of the red stinkwood *Prunus africana* Hook f. Kalkman (Rosaceae) that is used as a treatment for benign prostatic hypertrophy (Ishani et al., 2000); extracts from *Aloe vera* L. (Liliaceae), to treat burns and added to skin creams and cosmetics (Boudreau and Beland, 2006); the castor bean from *Ricinus communis* L. (Euphorbiaceae) which yields the laxative castor oil (Ogunniyi, 2006); and bark from *Pausinystalia yohimbe* Pierre ex Beille (Rubiaceae) that is in high demand as an over-the-counter herbal aphrodisiac in herbal extract form, and yields yohimbine that is useful against erectile dysfunction and female sexual arousal disorder (Adeniyi et al., 2007).

One of the first medicinal plants from South America that evoked broad interest in Europe was the quinine-containing tree *Cinchona officinalis* L. (Rubiaceae). Jesuit missionaries brought the bark of this plant at the beginning of the 1500s to Europe, where, by the 16$^{th}$ century, infusions were used to treat malaria and fever under the name 'Jesuit fever bark' (Wallace, 1996). More recent plant-derived medicines from South America, Central America, and the Caribbean are the anti-coagulant bromelaine, isolated from the juice of the pineapple *Ananas comosus* Mill. (Bromeliaceae; Gregory and Kelly, 1996) the muscarinic alkaloid pilocarpine obtained from the jaborandi tree *Pilocarpus jaborandi* Vahl (Rutaceae) that is useful against glaucoma (Rosin, 1991); and extracts from the leaves of the coca tree *Erythroxylum coca* Lam. (Erythroxylaceae), that yielded one of the first anesthetics in medicine and are now used, among others, as precursors for the local anesthetic drug procaine (Rivera et al., 2005).

## NEW DRUG DISCOVERY AND DEVELOPMENT IN THE REPUBLIC OF SURINAME

The Republic of Suriname is situated on the north-eastern coast of South America and has as its capital the city of Paramaribo. Its surface area of about 164,000 km$^2$ is located on the Guiana Shield, one of the regions with the highest biodiversity and the largest expanse of undisturbed tropical rain forest in the world (Hammond, 2005). This includes a minimum of 6,000 higher plant species (Hammond, 2005), at least 200 of which are used for medicinal purposes (Ministry of Agriculture, Animal husbandry, and Fisheries of Suriname, 1996).

Suriname's population of approximately 500,000 consists of a unique blend of ethnic groups, cultures, and religions

**Table 1.** Potential clinical value of a number of Surinamese medicinal plants.

| Scientific name (popular name) | Family | Potential clinical usefulness |
|---|---|---|
| *Annona muricata* L. (soursop) | Annonaceae | Hypertension (Mans et al., 2010) |
| *Artocarpus altilis* Forst. (bread fruit) | Moraceae | Hypertension (Mans et al., 2010) |
| *Averrhoa bilimbi* L. (bilimbi) | Oxalidaceae | Hypertension (Bipat et al., 2008) |
| *Bixa orellana* L. (annato) | Bixacaea | Spasmolytic (Mans et al., 2004 a) |
| *Caesalpinia pulcherrima* (L.) Schwartz (peacock flower) | Caesalpiniaceae | Spasmolytic (Mans et al., 2004 a) |
| *Commelina virginica* L. (virginia dayflower) | Commelinaceae | Hypertension (Mans et al., 2010) |
| *Cymbopogon citratus* Stapf. (lemon grass) | Graminae | Spasmolytic (Mans et al., 2004 a) |
| *Gossypium barbadense* L. (sea island cotton) | Malvaceae | Hypertension (Mans et al., 2010) |
| *Kalanchoë pinnata* (Lam.) Pers.(mother of thousands) | Crassulaceae | Spasmolytic (Mans et al., 2004 a) |
| *Phyllanthus amarus* Schum. & Thonn. (black catnip) | Euphorbiacaea | Hypertension (Bipat et al., 2008) |
| *Solanum melongena* L. (egg plant) | Solanaceae | Bronchospasmogenic (Mans et al., 2004 b)<br>Hypertension (Bipat et al., 2008) |
| *Tagetes erecta* L. (African marigold) | Compositae | Spasmolytic (Mans et al., 2004 a) |

from all continents, including Amerindians, the original inhabitants; Marroons, the immediate descendants of runaway slaves who had been shipped from Western Africa between the 17th and the 19th century; Creoles, a generic term referring to mixed blacks and whites; the descendants from contract workers attracted from China, India, and Java (Indonesia) between the second half of the 19th and the first half of the 20th century; as well as immigrants from Lebanon, Syria, various European countries, and Brazil (General Bureau of Statistics, 2012). All these groups have made their own specific contribution to Suriname's rich traditional medicine, which has resulted in a myriad of folk remedies against a wide variety of disorders.

Unfortunately, in the majority of cases there is little scientific evidence to support these claims of therapeutic efficacy. For this reason, the Faculty of Medical Sciences of the Anton de Kom University of Suriname has implemented a large-scale program to collect and evaluate Surinamese plants for their presumed medicinal properties. The initial focus of the program is on plants with a traditional use against cardiovascular, neoplastic, diabetic, and chronic obstructive airway disease. These conditions are among the most prevalent chronic disorders in many countries throughout the world including Suriname (Lopez et al., 2006).

## Plant collection and plant extraction

Considering Suriname's abundant plant biodiversity and cultural variety, candidate plants are primarily acquired on the basis of ethnopharmacological indications provided by Suriname's rich medicinal folklore. This information is supplemented by chemosystemic clues from the literature.

Plants are usually collected in Suriname's hinterland and in rural areas outside Paramaribo at locations that had been free of herbicides and pesticides for at least the previous six months. During each expedition, official guidelines are taken into account. Thus, each location is visited only twice a year, protected species are not collected, no trees are felled, samples of bark are taken from only one side and kept to a minimum, and root samples are only taken from the periphery. The collected samples are placed in boxes along with the complete taxonomy of the plant, date of collection, and geographical location as established by the Global Positioning System.

After authentication or – in the case of a new species, identification - by experts at the National Herbarium of Suriname, the samples are shipped to our extraction laboratory in Paramaribo. There, they are air-dried, macerated, and first soaked in an organic solvent such as chloroform to yield crude lipophilic extracts, then with distilled water to yield crude aqueous extracts. These are concentrated by rotary evaporation or lyophilization, respectively, weighed, labeled, and stored at -20°C until testing.

## Initial test results

Up till now, a few hundreds of crude plant extracts have been prepared and initially evaluated for one of the earlier-mentioned conditions using isolated animal organs, cultured human tumor cells, and zebra fish embryo's. Some of our initial results are presented in Table 1. Thus, aqueous extracts from *K. pinnata*, *C. citratus*, *C. pulcherrima*, and *B. orellana* were found to exhibit encouraging spasmolytic properties in isolated guinea pig ilei (Mans et al., 2004 a). On the other hand, contrary to folkloristic believe, a methanol extract from *S. melongena* leaves displayed a bronchospasmogenic rather than a bronchospasmolytic effect in isolated guinea pig trachea (Mans et al., 2004 b).

Furthermore, extracts from *S. melongena*, *P. amarus* and *A. bilimbi* reduced the cardiac output of norepinephrine-

stimulated isolated guinea pig atria, suggesting that they may lower an elevated blood pressure (Bipat et al., 2008). The same may hold true for extracts from *A. altilis*, *A. muricata*, *C. virginia*, and *G. barbadense*, which appeared to relax isolated guinea pig aorta rings pre-constricted with phenylephrine (Mans et al., 2010).

Currently, these positive plant extracts are being studied in more comprehensive pharmacological models to elucidate their precise mechanism of action, and investigations to isolate, purify, and elucidate their chemical structure are in preparation.

## CONCLUDING REMARKS

What are the provisions of new drug discovery and development programs such as those in Suriname? When considering that a successful drug can achieve worldwide annual commercial sales at a minimum of US$ 10 million (Fabricant and Farnsworth, 2001), and the presence of at least 200 plants with medicinal properties in Suriname (Ministry of Agriculture, Animal husbandry, and Fisheries of Suriname, 1996), the country's green resources have the potential to bring in a minimum of US$ 2 billion per annum. Even with a success rate of only 10%, revenues from plant-derived medicines may still amount to approximately US$ 200 million per year. This can substantially be increased by incomes from other economically profitable plant compounds such as oils, resins, gums, waxes, dyes, flavors, and fragrances.

Essential conditions for these provisions to become reality are the clever and conscious utilization, development, and maintenance of these resources, including practices aimed at biodiversity conservation; sustainable wild collection of medicinal plants with regard to the environment and to the long-term viability of plant species; and equitable sharing of revenues between the providers of the raw materials and the consumers of the finished products. The fulfillment of these prerequisites must eventually lead to a more advantageous exploitation of the astonishing pharmacopoeias of the green pharmacies of the world.

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