

Review

# Beneficial Properties and Sustainable Use of a Traditional Medicinal Plant: *Griffonia simplicifolia*

Amirhossein Nazhand <sup>1</sup>, Alessandra Durazzo <sup>2</sup>, Massimo Lucarini <sup>2,\*</sup>, Fabrizia Guerra <sup>3</sup>,  
Angélica Gomes Coêlho <sup>4</sup>, Eliana B. Souto <sup>5,6</sup>, Daniel Dias Rufino Arcanjo <sup>4</sup> and Antonello Santini <sup>7,\*</sup>

- <sup>1</sup> Department of Biotechnology, Sari Agricultural Science and Natural Resource University, 9th Km of Farah Abad Road, Sari 4818168984, Mazandaran, Iran; nazhand.ah@gmail.com
- <sup>2</sup> CREA-Research Centre for Food and Nutrition, Via Ardeatina 546, 00178 Roma, Italy; alessandra.durazzo@crea.gov.it
- <sup>3</sup> Inventia Biotech, Food Research Centre Healthcare, S.S. Sannitica 20.700th Km, 81020 Caserta, Italy; inventiabiotechsrl@gmail.com
- <sup>4</sup> Laboratory of Functional and Molecular Studies in Physiopharmacology (LAFMOL), Department of Biophysics and Physiology, Federal University of Piauí, Teresina 64049-550, Piauí, Brazil; angelicacoelho13@gmail.com (A.G.C.); daniel.arcanjo@ufpi.edu.br (D.D.R.A.)
- <sup>5</sup> Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, University of Porto, Rua de Jorge Viterbo Ferreira, 228, 4050-313 Porto, Portugal; souto.eliana@gmail.com
- <sup>6</sup> Applied Molecular Biosciences Unit (UCIBIO), Faculty of Pharmacy, University of Porto, Rua de Jorge Viterbo Ferreira, 228, 4050-313 Porto, Portugal
- <sup>7</sup> Department of Pharmacy, University of Napoli Federico II, Via D. Montesano 49, 80131 Napoli, Italy
- \* Correspondence: massimo.lucarini@crea.gov.it (M.L.); asantini@unina.it (A.S.)

**Abstract:** Since ancient times, medicinal plants have been a universal source of biologically active substances with high potential for the treatment of various diseases and disorders. For centuries, traditional communities have often relied on medicinal plants to treat health problems. Therefore, accurate information is required and knowledge about traditional medicinal plants requires evaluation, and great attention should be given to the possible integration of these plants as therapeutic agents or as complements to conventional pharmacological therapies in the healthcare system. Recently, *Griffonia simplicifolia* (DC.) Baill., initially used as a holistic remedy, has attracted attention from many researchers and consumers because of its multiple health-promoting effects. This growing interest prompted us to give an updated review of the botanical, geographical, historical, and therapeutic potentials of *Griffonia simplicifolia* (DC.) Baill. in terms of its in vitro and in vivo health effects, nutritional uses, and possible applications in line with biodiversity and sustainability concepts. This paper also presents a quantitative research analysis of the published studies related to this plant that are available in the literature. To retrieve the publications related to this plant, a bibliographic search was carried out using the Scopus database. The bibliometric data were extracted and processed using VOSviewer software (v.1.6.16, 2020). Technological possible applications in terms of patents request presented was also performed. A total of 1386 publications, from the year 1970 to the year 2021, were obtained by the literature search, and these had been collectively cited 38,805 times. The large amount of literature data available documents the interest in this plant's use as a tool for integrating traditional holistic healing approach, e.g., using plants, herbs, and holistic remedies, into the healthcare system as supporting tools and/or therapeutic agents, which is a current worldwide challenge.

**Keywords:** *Griffonia simplicifolia*; bioactive components; beneficial properties; in vitro studies; in vivo studies; literature quantitative research analysis; sustainability



**Citation:** Nazhand, A.; Durazzo, A.; Lucarini, M.; Guerra, F.; Coêlho, A.G.; Souto, E.B.; Arcanjo, D.D.R.; Santini, A. Beneficial Properties and Sustainable Use of a Traditional Medicinal Plant: *Griffonia simplicifolia*. *Challenges* **2024**, *15*, 14. <https://doi.org/10.3390/challe15010014>

Academic Editor: Susan Prescott

Received: 22 January 2024

Revised: 4 March 2024

Accepted: 6 March 2024

Published: 12 March 2024



**Copyright:** © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Medicinal plants have been utilized since ancient times as the main therapeutic approaches to the management of various diseases worldwide [1–4]. So far, about 50,000 to

80,000 herbs have been prescribed as medicine, according to the International Union for Conservation of Nature (IUCN) [5], in line with biodiversity and sustainability concepts [6–8]. Medicinal plants and their bioactive-molecule contents are natural sources of beneficial compounds that have been impacting human health on a planetary scale for thousands of years. Biodiversity and ecosystems with natural resources of commercial value have often been relevant in obtaining complete benefits of natural products to provide substances to be possibly used as remedies or in general health-beneficial substances. For this reason, an assessments should be performed evaluating the vulnerability of the ecosystems and at the same time also the critical points relevant to the environmental crisis that we are nowadays experiencing. From this point of view, medicinal plants are a relevant resource from a planetary health perspective, and *Griffonia simplicifolia* (DC.) Baill. can be considered an example of a less-used plant, notwithstanding its multiple health-promoting effects. These last effects would need to be fully studied and assessed in order to be capable of contributing properly to the overall social, economic, and environmental benefits that are the three pillars of sustainability, including developing the cultivation of native medicinal plants as resources that can limit global environmental change. The initial holistic approach of medicinal plant use, in fact, evolved into the use of plant phytocomplexes, e.g., developed into nutraceuticals, which can be used as support to conventional therapies, especially in those cases where the conventional pharmacological approach is difficult or not well tolerated. This aspect could trigger a transdisciplinary research framework approach capable of evaluating the use of natural medicinal resources instead or as a support, in some cases, of pharmaceuticals in therapeutic approach, depending on the health condition to be treated. The medicinal plants' biodiversity, and their contents of bioactive substances, could allow the setting of guidelines to help un decision making in promoting sustainable development, starting from global healthcare and considering the need to protect the natural habitat with respect to sustainability and having a minor environmental impact. This creates an interconnection with local and global ecologies and with the health of people and communities based on natural components of natural origin and beneficial health effects. This is becoming, nowadays, more and more relevant to the demands of users compared to conventional pharmaceuticals, and it represents one of the most interest triggering challenges for the research in the coming years.

*G. simplicifolia* (DC) Baill. [9] is a flowering herb belonging to the *Leguminosae* (*Fabaceae*) family with several health-promoting effects, including antioxidant, antimicrobial, and nephroprotective activity [10–13] as well as having efficacy in the management and treatment of depression, anxiety, migraines, headaches, and insomnia [14–16]. It grows in the tropical rainforests of the West and Central Africa, and it is also cultivated in Togo, Ivory Coast, and Ghana. *Griffonia simplicifolia* (DC) Baill. is also known by other botanical synonyms like *Bandeiraea simplicifolia* (DC.) Benth. and *Schotia simplicifolia* M. Vahl ex DC. Several parts of this medicinal plant have been administered using a traditional pure-holistic approach to manage different disorders. In particular, the leaf juice (for bladder and kidney diseases), leaves and stems (for wound healing, stop vomiting, and pelvic congestion), and the seeds (for diarrhea, stomachache, and dysentery) have been used [9].

The wide use of this plant and its parts has generated a great number of published studies in the current literature. Using the quantitative literature analysis approach, this manuscript also provides a current analysis of the most interesting, published studies on *Griffonia simplicifolia*. To assess the context of the proposed perspective study, a snapshot of the botanical, geographical, historical, and therapeutic potentials of *Griffonia simplicifolia* in terms of its in vitro and in vivo health effects, nutritional applications, is presented together with a focus on the main active substances present in the plant. Technological possible applications of patents related to this plant use have also been mentioned.

## 2. *Griffonia simplicifolia*: Quantitative Research Literature Analysis

This paper gives a current and comprehensive analysis of the *Griffonia simplicifolia* data present in the literature. On 30 October 2021, the Scopus database was used to carry

out a search in order to retrieve *Griffonia simplicifolia* publications. To extract bibliometric data, the following search strings in combination with the Boolean operator “OR” were used from the Scopus online database (<https://www.scopus.com/home.uri>, URL accessed on 30 October 2021): “*Griffonia simplicifolia*” OR “*Bandeiraea simplicifolia*” OR “*Schotia simplicifolia*”. The extracted bibliographic data were then recorded taking into consideration parameters such as year of publication, publication count, type of document (e.g., article, review, and book chapter), Institutions, and the countries/territories most productive in this field of research.

The features of the Scopus web platform called “Analyze” and “Create Citation report” were used to carry out the basic analyses, and for further bibliometric analyses VOSviewer software (version 1.6.16, [www.vosviewer.com](http://www.vosviewer.com), accessed on 30 October 2021) was used after importing the bibliometric research data relating to “complete records and cited references”.

To create and visualize the bubble map (“term map”), the words and terms used in the abstracts and titles of the publications were analyzed by VOSviewer software (version 1.6.16, [www.vosviewer.com](http://www.vosviewer.com), accessed on 30 October 2021) that linked them with publication citation data [17–19]. Default software parameters were used for analyses and visualizations. The output of the software is the “term map” in which the size of each bubble represents the frequency of appearance of a term coming from the bibliometric research. The relative positions of the bubbles depend on the frequency of appearance of the terms in the analyzed publications: the bubbles are closer if the terms co-appear more frequently in the research. Citations per publication are represented by the color of the bubble (citations per publication, CPP). This quantitative research analysis approach was carried out in previous researches on natural products [20–22].

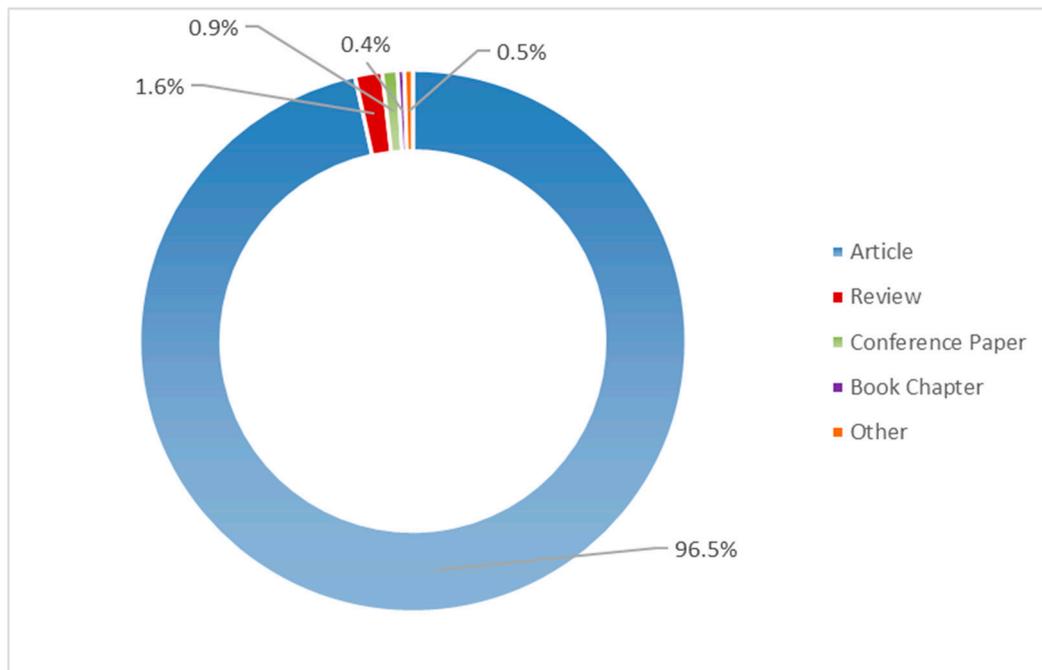
A large number of publications, namely 1386, dated from 1970 to 2021, were returned by the literature search and these had been collectively cited 38,805 times. The chosen minimum threshold for the keyword frequency was set to five in the VOSviewer software v1.6.16. Of the 10,467 keywords found, 1327 met the selected threshold, while 3 of them were manually excluded. A total of 1324 terms were identified from the quantitative literature search on 1386 publications. The results are displayed as a term map shown in Figure 1.

Publications and citation trends concerning *Griffonia simplicifolia* are reported in Figure 2. Among the oldest papers, it is worth mentioning the paper published in 1970 in *Phytochemistry* by Fellows and Bell [23], which described the isolation and identification of 5-hydroxytryptamine, 5-hydroxy-l-tryptophan, and l-tryptophan-5-hydroxylase in different parts of the *Griffonia simplicifolia* plant. The work of Hayes and Goldstein, reported the isolation, by affinity chromatography, and characterization of  $\alpha$ -D-galactosyl binding lectin from *B. simplicifolia* seeds [24]. The paper by Dwuma-Badu, published in 1976 entitled “constituents of West African medicinal plants. XVI. Griffonin and griffonilide, novel constituents of *G. simplicifolia*” [25] is another example.

The most recent work has been published by Cunningham et al. [26] in 2021 in the *Journal of Ethnopharmacology*, and it is entitled: “From forest to pharmacy: Should we be depressed about a sustainable *Griffonia simplicifolia* (Fabaceae) seed supply chain?”. The low habitat specificity and vigorous re-sprouting of *Griffonia simplicifolia* after cutting, plus its occurrence in forest reserves and national parks, confer some resilience on wild populations. This study is well presented with respect to the strict linkage existing between food and territory [27,28].

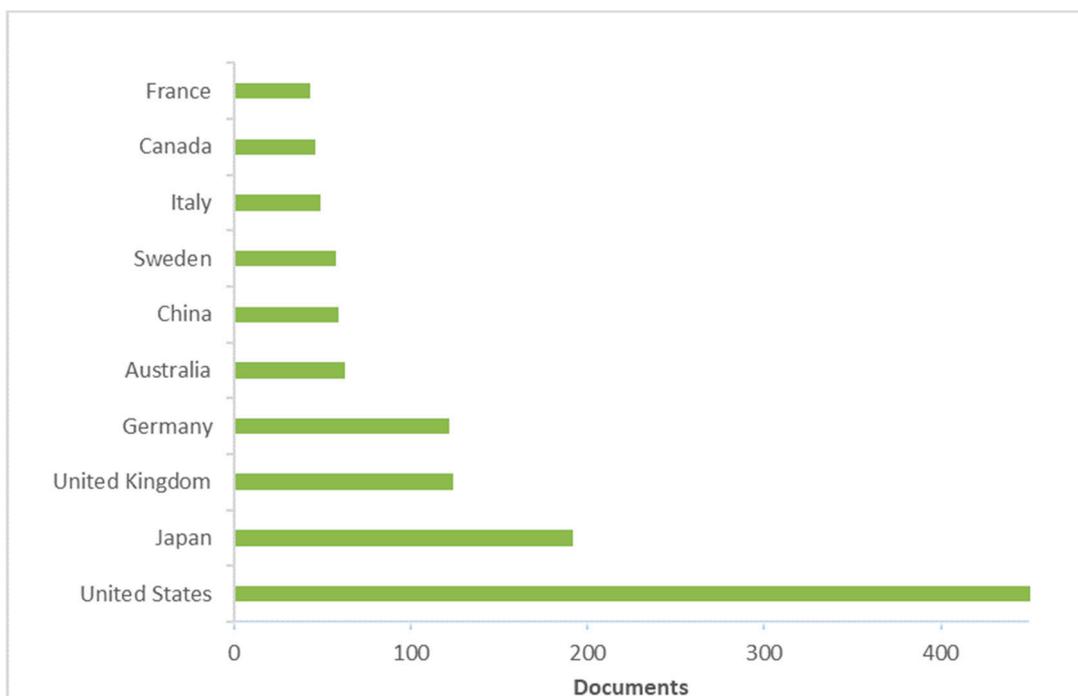
Figure 3 reports the distribution of documents displayed by type for the *Griffonia simplicifolia* publications. It includes mainly “Article” for 96.5% of documents, followed by “Review” at 1.6%, and “Conference paper” (0.9%).



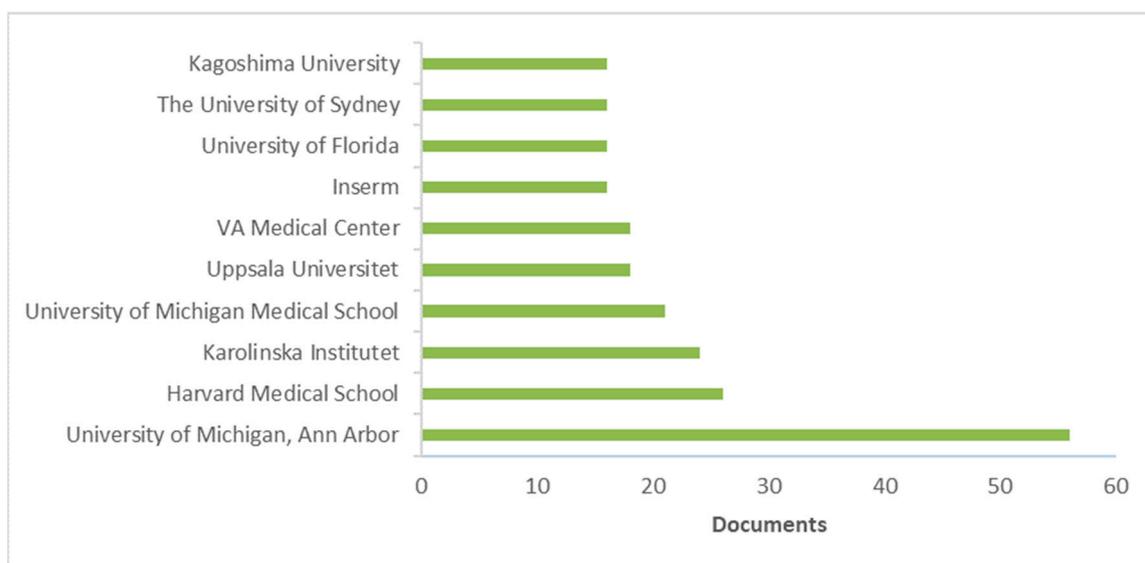


**Figure 3.** Distribution of documents by type for *Griffonia simplicifolia* publications (based on data from Scopus).

Figures 4 and 5 report, respectively, the most productive countries/territories and institutions. Regarding countries/territories, the United States ( $n = 529$ ) was the most productive country, followed by Japan ( $n = 192$ ) and the United Kingdom ( $n = 124$ ).



**Figure 4.** Most productive countries/territories (based on data from Scopus).



**Figure 5.** Most productive institutions (based on data from Scopus).

The most productive Institution was the University of Michigan, Ann Arbor ( $n = 56$ ). Each of the Top 10 Institutions contributed at least 16 publications.

### 3. The Botanical Aspects of *Griffonia simplicifolia*

*Griffonia simplicifolia* is a plant species belonging to the *Leguminosae* family. It is a flowering medicinal herb that is a woody and climbing large shrub. This medicinal plant can be up to three meters high, with greenish flowers and with leaves covering seeds about 1.7 cm in diameter and weighing 0.5 g. It is found mainly in West African Countries where it is present in the termite hills and foothills of the forest area in the sub-Saharan mountain slopes [29,30].

### 4. Ethnopharmacology and Traditional Medicinal Uses of *Griffonia simplicifolia*

Traditional medicine has benefitted from different parts of this plant for the treatment of various disorders, including: (i) the bark, for treating pelvic congestion and skin wounds; (ii) the leaves, for stopping vomiting and treating skin injuries, eye inflammation, and renal conditions; (iii) the roots and leaves, for treating sickle cell anemia, gonorrhea, stomach sick conditions, and lower pediatric fevers. In particular, traditional African medicine has for centuries been administrating different parts of *Griffonia simplicifolia* with various therapeutic purposes, in the forms of chewing small sticks of stems and roots or applying leaves to wounds for healing. The use of plant juice for treating urinary tract diseases or of decocts obtained from leaves and stems as antiemetic drugs is also part of traditional holistic remedies, as well as the use of different parts as antibiotics and even as aphrodisiacs as shown in Table 1.

**Table 1.** Main traditional medicinal uses of the *Griffonia simplicifolia*.

Region	Plant Parts	Traditional Uses	References
Africa	Leaves	Treatment of kidney and bladder ailments and skin diseases	[31]
Africa	Leaves	Wound healing	[32]
Africa	Decocts from stems and leaves	Antiemetic drugs	[32]

## 5. Main *Griffonia simplicifolia* Components Having Nutraceutical Potential

The diversity of compounds in plants is related to the infinite possible combinations of the main functional groups, i.e., hydroxyls, alcohols, aldehydes, alkyls, benzyl rings, and steroids that leads to compounds with their own chemical and physical properties, i.e., melting point, solubility, structure, and reactivity [33].

Identification, isolation, and quantification of bioactive compounds represent the main steps in plant studies. Some examples are described in the following text. The reported chemical composition of *Griffonia simplicifolia* includes major compounds as follows: lectins, fatty acids, and 5-hydroxy-L-tryptophan [34]. Koppiseti et al. [35] reported the presence of L-5-hydroxytryptophan (5-HTP) in the *Griffonia simplicifolia* seeds using the LC–MS technique with RSD of 97.00–100.20%, linearity range of 3–20 ng/L, LOQ of 0.05, and LOD of 0.02 ng/L [35]. In a recent study, a single-step seed extraction method was used to detect the chemical composition of *Griffonia simplicifolia*, the results of which identified the 5-Hydroxytryptophan as the main compound, which was confirmed by HPLC and solvent extraction procedures [36]. 5-HTP (5-Hydroxy-L-tryptophan) was identified in *Griffonia simplicifolia* seed extract by Kim et al. [37] using an HPLC/UV technique with an average value of  $15.7 \pm 0.63\%$  (*w/w*) and a range from 14.3 to 17.1% (*w/w*) [37]. Vigliante et al. [38] used an HPLC-DAD-ESI-MS/MS technique to analyze the *Griffonia simplicifolia* seed extract and reported 5-hydroxy-L-tryptophan (5-HTP) as the most abundant compound [38]. Table 2 summarizes the main active compounds identified in several parts of the plant and the analytical techniques that were used. The phytocomplex extracted from the plant could be a new nutraceutical to be screened and evaluated, considering the many beneficial health effects attributed to the active compounds contained in this plant. The possible risks to safety due to the plant's secondary metabolites [39] and possible contamination should be also taken into proper consideration [40–46].

**Table 2.** Examples of the main active compounds identified in different parts of the *Griffonia simplicifolia* plant and the analytical techniques used.

Compound	Plant Parts	Methodological and Analytical Approach	References
5-hydroxy-L-tryptophan (5-HTP)	seeds	HPLC-DAD-ESI-MS/MS	[38]
Apigenin-C-glycosides	leaves	HPLC, LC/MS and Mass spectroscopy	[47]
$\alpha$ -tocopherol and $\gamma$ -tocopherol	seeds	GC and HPLC	[47]
$\alpha$ -tocopherol and $\gamma$ -tocopherol	seeds	GC–MS and HPLC	[48]
$\alpha$ -tocopherol	seeds	GC–MS	[49]

Among the more interesting chemical compounds present in the *Griffonia simplicifolia* seeds, 5-hydroxy-L-tryptophan (5-HTP) has been reported as present. 5-HTP, the intermediate metabolite of the essential amino acid L-tryptophan, which is involved in the biosynthesis of serotonin (5-HT) and fatty acids, was extracted from the plant seed. Feng et al. [50] isolated the 5-HTP compound (with a purity of >99%) from the seeds of this plant through high selective adsorption using ion-exchange resins (loading solution flow rate = 4.0 mL/min, loading solution concentration = 10.8 mg/mL, and pH = 3.5) [50].

Various phytochemicals have been identified in the *Griffonia simplicifolia* leaf extract. As an example, a recent study used preparative thin-layer chromatography (TLC) using Sephadex LH-20 and silica gel to separate  $\beta$ -carboline alkaloid (griffonine), which was then confirmed by NMR and MS analytical techniques [51]. Many components of this plant have been separated using TLC and column chromatography (CC) methods, followed by analysis via Fourier transform infrared spectroscopy (FTIR), the results of which confirmed

the presence of saponins, steroids, flavonoids, tannins, phenols, coumarins, glycosides, triterpenoids, and alkaloids as well as 0.1–0.2% serotonin in the plant leaves [13].

## 6. In Vitro and In Vivo Therapeutic Potentials of *Griffonia simplicifolia*

In a plant, the determination of its phytochemical composition can be considered as the first step to suggest the health-promoting effects, and it is usually followed by the assessment of the structure of the chemical compounds involved in the possible health-related activities. Figure 6 indicates the main properties with benefits for health that are associated with the plant and possible applications in the treatment of different health conditions.



**Figure 6.** Scheme of the *Griffonia simplicifolia*'s potential beneficial properties.

### 6.1. Beneficial Activities of *Griffonia simplicifolia* Based on In Vitro Studies

Numerous reports are available for *Griffonia simplicifolia* extracts health beneficial effect with reference to their evaluation under in vitro conditions. A study applied thin-layer chromatography, column chromatography, and FTIR analysis to detect the chemical composition of *Griffonia simplicifolia* leaf petroleum ether and methanol extracts, and identified coumarins, saponins, triterpenoids, tannins, steroids, phenols, glycosides, flavonoids, glycosides, alkaloids, and flavonoids. The following antimicrobial activity testing reported minimum inhibition values (MIC) values of 12.5–62.5 mg/mL [13]. A study assessed the antioxidant activity of the aqueous *Griffonia simplicifolia* leaf extract (at a concentration of 20 µg/mL) via the protection of astrocytes and neurons [52]. In a recent study by Offoumou et al. the aqueous extracts of medicinal plants, especially *Griffonia simplicifolia*, exhibited antimalarial activity against *Plasmodium falciparum* [53]. Giurleo et al. [10] have evaluated flavone C-Glycosides and total antioxidant capacities in the leaves of eight wild *Griffonia simplicifolia* populations. Another study applied the HPLC method to measure the levels of hydroxytryptophan (5-HTP) present in *Griffonia simplicifolia* seeds gathered from different parts of Ghana and Liberia, as well as performing the 2,2'-azinobis-(3-ethylbenzthiazolin-6-sulfonic acid) assay to evaluate its antioxidant capacity [11]. According to the reported results, the 5-HTP content was between 110.23 mg/g and 137.04 mg/g, and the mean antioxidant activity was 216.51 mg of trolox equivalent antioxidant capacity (TEAC) in the range between 163.65 and 257.36 mg TEAC/g.

### 6.2. Health-Promoting Effects of *Griffonia simplicifolia* in Animals

Many studies conducted on animals have evaluated the health-promoting effects of *Griffonia simplicifolia* extracts. Nyarko et al. prescribed *Griffonia simplicifolia* leaf extract in rats with gentamicin/cisplatin-induced nephrotoxicity and observed nephroprotective effects due to the restoration of creatinine and urea concentrations to normal levels and the enhancement of glutathione peroxidase levels, as well as the reduction of nitric oxide levels [12]. The effects of 5-HTP (5-hydroxytryptophan) extracted from *Griffonia simplicifolia*

seed was evaluated in a study on sexual behavior [54]. The administration of 5-HTP (5-hydroxytryptophan) at a dose of 100 mg/kg/day for nine days to rats led to significant reductions in body weight and food intake as well as increases in 5-hydroxyindoleacetic acid and serotonin levels [55]. Some interesting observations are reported in Table 3.

**Table 3.** Examples of updated studies concerning *Griffonia simplicifolia* carried out in animals.

Effect	Extract/Compound Used	Experimental Design and Animal Model Used	Reference
Inhibition of locomotor activity	<i>Griffonia simplicifolia</i> /magnesium formulation	Taking <i>G. simplicifolia</i> -derived 5-HTP attenuated locomotor activity in mice.	[15]
Antioxidant effect	hydroethanolic leaf extract of <i>Griffonia simplicifolia</i> .	The platelet count and platelet-large cell ratio (P-LCR) were decreased, and the levels of blood glucose and low-density lipoproteins were elevated in a rat animal model.	[56]
Treatment of anxiety-related syndromes	<i>Griffonia simplicifolia</i> Baill. seed extract	The time spent in the central area of open field and in the light compartment of light/dark box was increased in the open field and light/dark box tests, respectively, in a rat animal model.	[57]
Antidepressant activity	<i>Griffonia simplicifolia</i> Aqueous Extracts	Immobility time was shortened in a tail suspension test (TST) by taking doses of 200 and 400 mg/Kg/day in rat animal model.	[58]

### 6.3. Beneficial Activities of *Griffonia simplicifolia* in Humans, with Particular Regard to Clinical Trials

Many clinical trials investigated the therapeutic potential of *Griffonia simplicifolia* extracts. Esposito et al. [59] prescribed the *Griffonia simplicifolia*/magnesium complex twice a day for three months to prepubertal children (group A) in comparison with a control group (B), and they found that some factors were lower in Group A than in Group B, including visual analogue scale values (2.59–0.14 versus 7.42–1.05;  $p < 0.001$ ), motion sickness (MS)-symptom severity (2.59–0.14 versus 6.91–2.08;  $p < 0.001$ ), and prevalence (36% versus 73%;  $p < 0.001$ ), thereby introducing the role of *Griffonia simplicifolia*/magnesium complex in the control of MS. In another study, they prescribed *Griffonia simplicifolia* extract and ginkgolide (a diterpenoid trilactone isolated from the tree *Ginkgo biloba*) for two separate groups of participants twice a day for six months, the results of which showed a significant difference in behavioral reactions to headache, Pediatric Migraine Disability Assessment Scale (Ped-MIDAS) score, headache frequency, duration, and intensity between the two groups [59]. In a study carried out by Rondanelli et al. [60], the administration of 5-hydroxytryptophan extracted from *G. simplicifolia* for a month elevated the satiety feeling by decreasing BMI in overweight females [60]. In another study developed by Pizza et al., *Griffonia simplicifolia* was co-prescribed with Vitamin PP, Vitamin B6, and L-tryptophan in children with migraines, which resulted in acceptable tolerability and low drug intake during acute attacks as well as in a reduction in headache-attack intensity and frequency [61]. A clinical trial using 60 mg of L-5-hydroxytryptophan extracted from *Griffonia simplicifolia* (containing 12.8 mg of 5-HTP) has been administered for six weeks to 15 patients with relationship problems or break-up issues in long-term relationship. The results showed significant elevation of both brain-derived neurotrophic factor (BDNF) and platelet serotonin levels compared to baseline values, suggesting the use of direct modulation of the serotonergic

system for the treatment of psychological suffering related to unreciprocated *romantic love* [62]. Additional interesting results that were obtained are summarized in Table 4.

**Table 4.** Example of updated studies concerning *Griffonia simplicifolia* carried out in humans, with particular regard to clinical trials.

Effect	Mechanism	Ref
Management of migraine aura symptoms	Taking Aurastop <sup>®</sup> as a novel tool containing magnesium pidolatatum (185 mg), <i>Griffonia simplicifolia</i> -derived 5-HTP (20 mg), <i>Tanacetum parthenium</i> extract (150 mg extracted at 0.8% = 1.2 mg of active parthenolide) decreased the duration of aura, aura-associated disability, headache episodes, pain intensity, and somatosensory presentations.	[63]
Treatment of Migraine Aura	Administration of (Aurastop <sup>®</sup> , Æsculapius Farmaceutici S.r.l., Brescia, Italy) in patients with a diagnosis of migraine with aura reduced disability degree and aura duration	[64]
Treatment of pediatric patients with headache	Co-administration of <i>Tanacetum parthenium</i> , <i>Griffonia simplicifolia</i> , and magnesium led to the reduction of the six-item Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS) score	[65]

## 7. Technological Prospecting

To search for patents relating to the term “*Griffonia simplicifolia*”, several databases were consulted: the European Patent Office (EPO, available at <https://register.epo.org/regviewer>, accessed on 30 October 2021), the World Intellectual Property Organization (WIPO, available at <https://www.wipo.int/portal/en/index.html>, accessed on 30 October 2021) and the United States Patent and Trademark Office (USPTO, available at <https://www.uspto.gov/>, accessed on 30 October 2021) and its Portuguese translations in the database of the Brazilian National Institute for Industrial Property (INPI, available at <https://www.gov.br/inpi/en>, accessed on 30 October 2021). The search was carried out using the term “*Griffonia simplicifolia*” in association with the words “property”, “therapeutic”, “treatment”, or “nutritional” used in the search field of each database consulted. The technological prospecting excluded products with exclusively cosmetic purposes or that report agricultural applications related to this species, as well as those that used derivatives of *Griffonia simplicifolia* for diagnostic purposes. This usage occurs due to the lecithins found in plant seeds that have site-specific molecular binding and allow the detection of distinct cell types, such as tumor stem cells.

Table 5 shows the patents filed using *G. simplicifolia* as a component of drug or food formulations, which were aiming to take advantage of its biological properties, especially in combating obesity, anxiety, and depression.

**Table 5.** Patents employing *Griffonia simplicifolia*, main products claimed, and related therapeutic applications.

Patent Title	Claimed Product	Therapeutic Application	Ref
Composition and method for enhancing neuromuscular facilitation and cognitive functions	Dietary supplement	Enhancing neuromuscular facilitation	[66]
Protein dietary supplement	Dietary supplement	Antidepressant	[67]
Appetite suppressant toothpaste	Toothpaste	Suppressing appetite	[68]
Dietary supplement for suppressing appetite, enhancing and extending satiety, improving glycemic control, and stimulant free	Dietary supplement	Suppressing appetite	[69]
Medicine for treating and adjusting depression and products for preparation of medicine.	Medicine	Antidepressant	[70]
Composition comprising at least one higher-aliphatic alcohol and an extract of <i>Griffonia simplicifolia</i>	Medicine or dietary supplement	Obesity	[71]
Compositions for the treatment of anxiety and associated disorders	Medicine or dietary supplement or cosmetic	Anxiety	[72]
Nutritional supplement for treatment of syndromes related to fatigue, including pain, muscular problems, anxiety, depression, and periods of fatigue	Dietary supplement	Muscle fatigue, anxiety, and depression	[73]
Nutritional healthcare green bean eight-treasure rice pudding	Dietary supplement	Cough and excessive phlegm, hypertension and liver problems.	[74]
Liquid mixture for electronic devices	Medicine	Anxiolytic	[75]
Food supplement assistant in diseases of the digestive tract also with any anxious-depressive component.	Dietary supplement	Dyspepsia anxiety depression	[76]
Compositions comprising plant extracts and use thereof for treating inflammation	Medicine or dietary supplement	Treating inflammation	[77]
Nutritional supplements affecting mood state and sleep quality	Dietary supplement	Improve mood and sleep	[78]
Compositions for relieving symptoms of menopausal syndrome	Medicine, dietary supplement, or cosmetic	Symptoms of menopausal	[79]
Weight loss composition and method of inducing weight loss	Dietary supplement	Obesity	[80]
Formulations comprising arginine and/or a pharmaceutically acceptable salt thereof and an acid active ingredient with a Pka of 1–5	Dietary supplement	Arginine food supplement enriched with plant extracts	[81]
Use of e.g., selective serotonin reuptake inhibitors, noradrenaline reuptake inhibitors, noradrenaline and dopamine reuptake inhibitors, and tricyclic or tetracyclic antidepressants to produce drugs for the treatment of lovesickness	Medicine	Antidepressant	[82]
Equol-enriched plant extract obtainable by fermentation	Dietary supplement	Symptoms of menopausal	[83]

Table 5. Cont.

Patent Title	Claimed Product	Therapeutic Application	Ref
Food composition and its use in the treatment of sleep disorders	Dietary supplement	Sleep disorders	[84]
Controlled-release formulations containing tryptophan and/or 5-hydroxytryptophan	Medicine	Antidepressant	[85]
Therapeutic association for the treatment of Parkinson's disease.	Medicine	Parkinson's disease.	[86]
Methods and materials for treating depression and mood disorder	Medicine or dietary supplement	Antidepressant	[87]
Food and/or nutraceutical composition containing pea	Dietary supplement	Treating inflammation	[88]

Such activities are explored through the formulation of dietary supplements, claimed in 74% of the analyzed patents, not excluding the possibility of drug development in 43% of the publications. All patents analyzed used the extract derived from the plant species, in many cases in association with extracts from other plant species [75,79,81] or with isolated pharmacological actives [82].

It is noteworthy that the presence of innovative formulations, such as appetite suppressant toothpaste, which simultaneously suppresses users' appetite while promoting intraoral cleansing, were found [68]. Also detected was a liquid mixture for electronic devices, such as electronic cigarettes, which uses plant extracts, including *Griffonia simplicifolia*, comprising, among others, sedative, anxiolytic, digestive, and satietogenic effects [75].

## 8. Conclusions and Future Remarks

Medicinal plants can be candidates for playing a pivotal role in managing and preventing the onset of diseases of public health importance, in particular with regard to their potential in strategic approaches for disease prevention and even therapy, especially when the conventional pharmacological approach is not well tolerated or individuals cannot qualify for it. For this reason, efforts should be addressed to the identification and assessment of recognized roles of medicinal plants in order to implement prevention and therapeutic strategies. This approach is nowadays requested by the users who search for "all natural" remedies, and this also has impacts on sustainability and global health management issues regarding the emerging perspectives of preventive strategies, as well as involving primary healthcare principles on a planetary scale.

*Griffonia simplicifolia* (DC.) Baill. is a medicinal plant that contains several biologically active natural compounds with therapeutic potential, and it is widely used to treat different disorders. The correlation between the chemical composition of this plant and the molecular targets involved in the treatment of diseases, as well as conclusions about the effects and consequences of long-term use of this plant, should be determined by more comprehensive in vitro and in vivo studies and, most importantly, by further clinical trials that are needed to assess its overall mechanisms of action. Studies conducted on animals gave important insights into pharmacokinetic properties and can help with the investigation of the beneficial health effects of this plant in humans. Due to its health-promoting effects, the phytocomplex of this plant may potentially be used as a tool in the nutraceutical arsenal for the prevention of the onset of some of the above-mentioned pathologic health conditions before there is need of a pharmacological treatment, in particular for subjects who do not qualify for a conventional pharmacological treatment. As an example, the 5-HTP precursor of the neurotransmitter serotonin, which is commercially obtained from the plant's seeds but cannot be patented as a pharmaceutical or nutraceutical, is present on the market as a food supplement according to the existing regulations. Nonetheless, it should be noted also that various unwanted effects have been reported for the administration of *Griffonia simplicifolia* (DC.) Baill. despite its health-promoting effects. Moreover, intellectual protection

was detected for the commercial exploitation of different formulations of medicines and foods containing the extract of *Griffonia simplicifolia* (DC.) Baill. Claiming, in particular, the possible therapeutic applications for obesity, anxiety, and depression. On the other hand, although pharmaceutical companies may have a profit justification for marketing these natural plant extracts, much research seems to be still needed for developing clinical trials and for assessing the following: (i) the mechanisms of action; (ii) the effective therapeutic dose; and (iii) the proper pharmaceutical formulation that should be administered for the treatment and/or the prevention of diseases to take advantage of the great therapeutic potential of this plant.

**Author Contributions:** All authors: A.N., A.D., M.L., F.G., A.G.C., E.B.S., D.D.R.A. and A.S. have equally contributed to this article. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Data Availability Statement:** The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding authors.

**Conflicts of Interest:** A.N., A.D., M.L., A.G.C., E.B.S., D.D.R.A. and A.S. declare no conflicts of interest. F.G. declares that there is no commercial or financial relationships that could be construed as a potential conflicts of interest considering that she currently collaborates with Inventia Biotech, Food research centre Healthcare.

## References

- Salehi, B.; Abu-Reidah, I.M.; Sharopov, F.; Karazhan, N.; Sharifi-Rad, J.; Akram, M.; Daniyal, M.; Khan, F.S.; Abbaass, W.; Zainab, R.; et al. *Vicia* plants—A comprehensive review on chemical composition and phytopharmacology. *Phytother. Res.* **2021**, *35*, 790–809. [[CrossRef](#)] [[PubMed](#)]
- Salehi, B.; Ata, A.V.; Anil Kumar, N.; Sharopov, F.; Ramírez-Alarcón, K.; Ruiz-Ortega, A.; Abdulmajid Ayatollahi, S.; Valere Tsouh Fokou, P.; Kobarfard, F.; Amiruddin Zakaria, Z. Antidiabetic potential of medicinal plants and their active components. *Biomolecules* **2019**, *9*, 551. [[CrossRef](#)] [[PubMed](#)]
- Salehi, B.; Sener, B.; Kilic, M.; Sharifi-Rad, J.; Naz, R.; Yousaf, Z.; Mudau, F.N.; Fokou, P.V.T.; Ezzat, S.M.; El Bishbishy, M.H. *Dioscorea* plants: A genus rich in vital nutra-pharmaceuticals—A review. *Iran. J. Pharm. Res. IJPR* **2019**, *18*, 68.
- Pagano, E.; Souto, E.B.; Durazzo, A.; Sharifi-Rad, J.; Lucarini, M.; Souto, S.E.; Salehi, B.; Zam, W.; Montanaro, V.; Lucariello, G.; et al. Ginger (*Zingiber officinale* Roscoe) as a nutraceutical: Focus on the metabolic, analgesic, and antiinflammatory effects. *Phytother. Res. Eng.* **2020**, *35*, 2403–2417. [[CrossRef](#)] [[PubMed](#)]
- Guarino, R.; Pignatti, S. Diversitas and biodiversity: The roots of a twenty-first century myth. *Rend. Lincei* **2010**, *21*, 351–357. [[CrossRef](#)]
- Pignatti, S.; Cipriani, M. The diversity of plants in a text from the seventeenth century. *Rend. Lincei* **2010**, *21*, 343–350. [[CrossRef](#)]
- Pignatti, S. A discussion on the foundations of environmental ethics. *Rend. Lincei* **2023**, *24*, 89–94. [[CrossRef](#)]
- Chen, S.-L.; Yu, H.; Luo, H.-M.; Wu, Q.; Li, C.-F.; Steinmetz, A. Conservation and sustainable use of medicinal plants: Problems, progress, and prospects. *Chin. Med.* **2016**, *11*, 37. [[CrossRef](#)]
- Balogun, M.M.; Jimoh, M.O.; Ogundipe, O.T. Conservation of a Rare Medicinal Plant: A Case Study of *Griffonia simplicifolia* (Vahl ex DC) Baill. *Eur. J. Med.* **2020**, *31*, 152–160. [[CrossRef](#)]
- Giurleo, D.J.; Juliani, H.R.; Amekuse, L.S.; Asante Dartey, J.; Simon, J.E.; Wu, Q. Flavone C-Glycosides and Total Antioxidant Capacities in Leaves of Eight Wild *Griffonia simplicifolia* Populations. In *African Natural Plant Products, Volume III: Discoveries and Innovations in Chemistry, Bioactivity, and Applications*; American Chemical Society: Washington, DC, USA, 2020; pp. 249–264.
- Giurleo, D.J.; Juliani, H.R.; Amekuse, L.S.; Dartey, J.A.; Wu, Q.; Simon, J.E. 5-HTP (5-Hydroxy-L-tryptophan) Content and Antioxidant Capacities of Wild *Griffonia simplicifolia* Seed Populations from Ghana and Liberia. In *African Natural Plant Products, Volume III: Discoveries and Innovations in Chemistry, Bioactivity, and Applications*; American Chemical Society: Washington, DC, USA, 2020; pp. 239–247.
- Nyarko, R.A.; Larbie, C.; Anning, A.K.; Baidoo, P.K.; Emikpe, B.O.; Oyagbemi, A.A.; Jarikre, T.A. *Griffonia simplicifolia* (DC.) Baill. attenuates gentamicin and cisplatin-induced nephrotoxicity in rats. *Compar. Clin. Pathol* **2019**, *28*, 1293–1304. [[CrossRef](#)]
- Akoto, C.O.; Acheampong, A.; Tagbor, P.D.; Bortey, K. Determination of the antimicrobial and antioxidant activities of the leaf extracts of *Griffonia simplicifolia*. *J. Pharmacogn. Phytochem.* **2020**, *9*, 537–545.
- Vicariotto, F.; Porchetti, A.; Murina, F.A. Dietary Supplement of Vitamin B6 with Four Herbal Extracts Improves Sleep Disturbances and Anxiety Associated with the Menstrual Cycle and Menopause Transition: Results from an Exploratory Study. *J. Name Integr. Complement. Ther.* **2022**, *28*, 265–269. [[CrossRef](#)]

15. Esposito, M.; Precenzano, F.; Sorrentino, M.; Avolio, D.; Carotenuto, M. A medical food formulation of *Griffonia simplicifolia*/magnesium for childhood periodic syndrome therapy: An open-label study on motion sickness. *J. Med. Food* **2015**, *18*, 916–920. [[CrossRef](#)] [[PubMed](#)]
16. De Melo Guerra Ribas, R.; Lopes de Oliveira, D.C.; César da Silva, P.; André de Lima Martins, H.; Gomes de Moraes, J. The different roles of *Griffonia simplicifolia* in the treatment of depression: A narrative review. *Int. J. Complement. Altern. Med.* **2021**, *14*, 167–171. [[CrossRef](#)]
17. Van Eck, N.J.; Waltman, L. Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics* **2010**, *84*, 523–538. [[CrossRef](#)] [[PubMed](#)]
18. Van Eck, N.J.; Waltman, L. Text mining and visualization using VOSviewer. *arXiv* **2011**, arXiv:1109.2058. [[CrossRef](#)]
19. Waltman, L.; Van Eck, N.J.; Noyons, E.C. A unified approach to mapping and clustering of bibliometric networks. *J. Inform.* **2011**, *4*, 629–635. [[CrossRef](#)]
20. Yeung, A.W.K.; Tzvetkov, N.T.; El-Tawil, O.S.; Bungău, S.G.; Abdel-Daim, M.M.; Atanasov, A.G. Antioxidants: Scientific Literature Landscape Analysis. *Oxid. Med. Cell. Longev.* **2019**, *2019*, 8278454. [[CrossRef](#)]
21. Durazzo, A.; Nazhand, A.; Lucarini, M.; Silva, A.M.; Souto, S.B.; Guerra, F.; Severino, P.; Zaccardelli, M.; Souto, E.B. *Astragalus (Astragalus membranaceus Bunge)*: Botanical, geographical, and historical aspects to pharmaceutical components and beneficial role. *Rend. Lincei Sci. Fis. Nat.* **2021**, *32*, 625–642. [[CrossRef](#)]
22. Durazzo, A.; Lucarini, M.; Nazhand, A.; GCoêlho, A.G.; ESouto, E.B.; Daniel DR Arcanjo, D.D.T.; Santini, A. *Rhodiola rosea*: Main features and its beneficial properties. *Rend. Lincei Sci. Fis. Nat.* **2022**, *33*, 71–82. [[CrossRef](#)]
23. Fellows, L.E.; Bell, E.A. 5-Hydroxy-L-tryptophan, 5-hydroxytryptamine and L-tryptophan-5-hydroxylase in *Griffonia simplicifolia*. *Phytochemistry* **1970**, *9*, 2389–2396. [[CrossRef](#)]
24. Hayes, C.E.; Goldstein, I.J. An  $\alpha$  D galactosyl binding lectin from *Bandeiraea simplicifolia* seeds. Isolation by affinity chromatography and characterization. *J. Biol. Chem.* **1974**, *249*, 1904–1914. [[CrossRef](#)]
25. Dwuma-Badu, D. Constituents of West African medicinal plants. XVI. *Griffonin* and *griffonilide*, novel constituents of *Griffonia simplicifolia*. *Lloydia* **1976**, *39*, 385–390. [[PubMed](#)]
26. Cunningham, A.B.; Brinckmann, J.A.; Harter, D.E.V. From forest to pharmacy: Should we be depressed about a sustainable *Griffonia simplicifolia* (Fabaceae) seed supply chain? *J. Ethnopharmacol.* **2021**, *278*, 114202. [[CrossRef](#)] [[PubMed](#)]
27. Durazzo, A.; Lucarini, M.; Zaccardelli, M.; Santini, A. Forest, Foods, and Nutrition. *Forests* **2020**, *11*, 1182. [[CrossRef](#)]
28. Durazzo, A. The Close Linkage between Nutrition and Environment through Biodiversity and Sustainability: Local Foods, Traditional Recipes, and Sustainable Diets. *Sustainability* **2019**, *11*, 2876. [[CrossRef](#)]
29. Kumar, P.S.; Praveen, T.; Jain, N.; Jitendra, B. A review on *Griffonia simplicifolia*-an ideal herbal anti-depressant. *Int. J. Pharm. Life Sci. IJPLS* **2010**, *1*, 174–181.
30. Kokou, K.; Adjossou, K.; Kokutse, A.D. Considering sacred and riverside forests in criteria and indicators of forest management in low wood producing countries: The case of Togo. *Ecol. Indic.* **2008**, *8*, 158–169. [[CrossRef](#)]
31. Tuo, K.; Bolou, G.E.K.; N'docho, A.F.T.; Chevillot, A.; Mammeri, M.; Vallee, I.; Adjou, K.; Toire, O.A.; Polack, B.; Jambou, R. Ethnobotanical Study of Plants Used in Traditional Treatment of Diarrhoea in Humans and Cattle in Two Regions of Ivory Coast. *Eur. J. Med. Plants* **2020**, *31*, 24–33. [[CrossRef](#)]
32. Brendler, T.; Eloff, J.N.; Gurib-Fakim, A.; Phillips, L. *African Herbal Pharmacopoeia*; Thomas Brendler, T., Jacobus, N., Eloff, J.N., Ameenah Gurib-Fakim, A., Phillips, D., Eds.; Association for African Medicinal Plants Standards; Graphic Press Ltd.: Port Louis, Mauritius, 2010; ISBN 9789990389098.
33. Roessner, U.; Beckles, D.M. Metabolite measurements. In *Plant Metabolic Networks*; Schwender, J., Ed.; Springer: New York, NY, USA, 2009; pp. 39–69. ISBN 9780387787459.
34. Muszyńska, B.; Łojewski, M.; Rojowski, J.; Opoka, W.; Sułkowska-Ziaja, K. Natural products of relevance in the prevention and supportive treatment of depression. *Psychiatr. Pol.* **2015**, *49*, 435–453. [[CrossRef](#)]
35. Koppiseti, G.; Siriki, A.; Sukala, K.; Subbaraju, G.V. Estimation of L-5-hydroxytryptophan in rat serum and *Griffonia* seed extracts by liquid chromatography–mass spectrometry. *Anal. Chim. Acta* **2005**, *549*, 129–133. [[CrossRef](#)]
36. Lemaire, P.A.; Adosraku, R.K. An HPLC method for the direct assay of the serotonin precursor, 5-hydroxytryptophan, in seeds of *Griffonia simplicifolia*. *Phytochem. Anal.* **2002**, *13*, 333–337. [[CrossRef](#)] [[PubMed](#)]
37. Kim, K.S.; Juliani, H.R.; Bucuk, M.; Acquaye, D.; Asante-Dartey, J.; Wu, Q.; Simon, J.E. Quality control and 5-HTP (5-Hydroxy-L-tryptophan) Analysis of *Griffonia* (*Griffonia simplicifolia* (DC.) Baill.) seed accessions collected in Ghana. In *ACS Symposium Series*; Oxford University Press: Oxford, UK, 2009; pp. 381–390.
38. Vigilante, I.; Mannino, G.; Maffei, M.E. Chemical Characterization and DNA Fingerprinting of *Griffonia simplicifolia* Baill. *Molecules* **2019**, *24*, 1032. [[CrossRef](#)] [[PubMed](#)]
39. Jędrejko, K.; Lazur, J.; Muszyńska, B. Risk Associated with the Use of Selected Ingredients in Food Supplements. *Chem. Biodivers.* **2021**, *18*, e2000686. [[CrossRef](#)] [[PubMed](#)]
40. Santini, A.; Ferracane, R.; Somma, M.C.; Aragón, A.; Ritieni, A. Multitoxin extraction and detection of trichothecenes in cereals: An improved LC-MS/MS approach. *J. Sci. Food Agric.* **2009**, *89*, 1145–1153. [[CrossRef](#)]
41. EFS. Compendium of botanicals reported to contain naturally occurring substances of possible concern for human health when used in food and food supplements. *EFSA J.* **2012**, *10*, 2663. [[CrossRef](#)]

42. Mikušová, P.; Šrobárová, A.; Sulyok, M.; Santini, A. *Fusarium* fungi and associated metabolites presence on grapes from Slovakia. *Mycot. Res.* **2013**, *29*, 97–102. [CrossRef]
43. Vieira, R.; Souto, S.B.; Sánchez-López, E.; López Machado, A.; Severino, P.; Jose, S.; Santini, A.; Fortuna, A.; García, M.L.; Silva, A.M. Sugar-lowering drugs for type 2 diabetes mellitus and metabolic syndrome—Review of classical and new compounds: Part-I. *Pharmaceuticals* **2019**, *12*, 152. [CrossRef]
44. Vieira, R.; Souto, S.B.; Sánchez-López, E.; López Machado, A.; Severino, P.; Jose, S.; Santini, A.; Silva, A.M.; Fortuna, A.; García, M.L. Sugar-lowering drugs for type 2 diabetes mellitus and metabolic syndrome—Strategies for in vivo administration: Part-II. *J. Clin. Med.* **2019**, *8*, 1332. [CrossRef]
45. Durazzo, A. Study Approach of Antioxidant Properties in Foods: Update and Considerations. *Foods* **2017**, *6*, 17. [CrossRef] [PubMed]
46. Durazzo, A.; Lucarini, M.; Santini, A. Nutraceuticals in Human Health. *Foods* **2020**, *9*, 370. [CrossRef]
47. Giurleo, D. A Phytochemical Exploration of *Griffonia simplicifolia* Seeds and Leaves. Master's Thesis, Rutgers The State University of New Jersey, Piscataway, NJ, USA, 2017. [CrossRef]
48. Mitei, Y.; Ngila, J.; Yeboah, S.; Wessjohann, L.; Schmidt, J. Profiling of phytosterols, tocopherols and tocotrienols in selected seed oils from Botswana by GC-MS and HPLC. *J. Am. Oil Chem. Soc.* **2009**, *86*, 617–625. [CrossRef]
49. Zhang, R.; Shen, W.; Wei, X.; Zhang, F.; Shen, C.; Wu, B.; Zhao, Z.; Liu, H.; Deng, X. Simultaneous determination of tocopherols and tocotrienols in vegetable oils by GC-MS. *Anal. Methods* **2016**, *8*, 7341–7346. [CrossRef]
50. Feng, J. Isolation and purification of 5-hydroxytryptophan in extract from seeds of *Griffonia simplicifolia* by ion-exchange resin. *Zhongcaoyao* **2013**, *44*, 2410–2415.
51. Xin-Zhi, W.; Fei-Hua, W.; Wei, Q.; Liang, J.-Y. A new  $\beta$ -carboline alkaloid from the seeds of *Griffonia simplicifolia*. *Chin. J. Nat. Med.* **2013**, *11*, 401–405.
52. Rolland, K.G.; Pandey, H.S.; Rostand, O.M.b.; Vini, T.; Diane, K.; Priyanka, S.; Joseph, D.A.; Seth, P. Cytoprotective action of *Griffonia simplicifolia* (DC.) Baill. against the oxidative stress caused by hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) on neurons and astrocytes. *GSC Bio. Pharm. Sci.* **2018**, *5*, 6–12.
53. Offoumou, M.; Kipre, G.; Kigbafori, D.; Camara, D.; Djaman, A.; Zirih, G. In vitro/ex vivo antiplasmodial activity and phytochemical screening of crude extracts *Entandrophragma angolense* (Welw.) C. DC., *Griffonia simplicifolia* (Vahl ex DC.) Baill. et *Uapaca guineensis* Müll. Arg. three plants of Ivorian pharmacopeia in treatment of malaria. *Int. J. Curr. Microb. App. Sci.* **2018**, *7*, 2088–2095.
54. Carnevale, G.; Di Viesti, V.; Zavatti, M.; Benelli, A.; Zanolli, P. Influence of *Griffonia simplicifolia* on male sexual behavior in rats: Behavioral and neurochemical study. *Phytomedicine* **2011**, *18*, 947–952. [CrossRef]
55. Aduema, W.; Amah, A.; Izunwanne, D. Inhibitory effect on Locomotor behaviour following chronic administration of 5-Hydroxytryptophan in the open field maze task. *Exper. Anim.* **2017**, *3*, 1–9.
56. Nyarko, R.A.; Larbie, C.; Anning, A.K.; Baidoo, P.K. Phytochemical constituents, antioxidant activity and toxicity assessment of hydroethanolic leaf extract of *Griffonia simplicifolia*. *Int. J. Phytopharmacol.* **2019**, *10*, 6–18.
57. Carnevale, G.; Di Viesti, V.; Zavatti, M.; Zanolli, P. Anxiolytic-like effect of *Griffonia simplicifolia* Baill. seed extract in rats. *Phytomedicine* **2011**, *18*, 848–851. [CrossRef]
58. François, B.N.; Abdoulaye, B.; Diabaté, D.; Atayi, E. Evaluation of the Antidepressant Activity of *Griffonia simplicifolia* Aqueous Extracts. *Sch. Int. J. Tradit. Complement. Med.* **2020**, *3*, 125–130. [CrossRef]
59. Esposito, M.; Ruberto, M.; Pascotto, A.; Carotenuto, M. Nutraceutical preparations in childhood migraine prophylaxis: Effects on headache outcomes including disability and behaviour. *Neuro. Sci.* **2012**, *33*, 1365–1368. [CrossRef] [PubMed]
60. Rondanelli, M.; Opizzi, A.; Faliva, M.; Bucci, M.; Perna, S. Relationship between the absorption of 5-hydroxytryptophan from an integrated diet, by means of *Griffonia simplicifolia* extract, and the effect on satiety in overweight females after oral spray administration. *Eat. Weight. Disord. -Stud. Anorex. Bulim. Obes.* **2012**, *17*, e22–e28.
61. Pizza, V.; Busillo, V.; Cassano, D.; Agresta, A.; d'Amato, C.C.; Capasso, A. Efficacy and Tolerability of a combination product with L-Tryptophan, *Griffonia simplicifolia*, Vitamin PP and Vitamin B6 in pediatric migraine prophylaxis: An open study. *Pharmacologyonline* **2013**, *2*, 23–27.
62. Emanuele, E.; Bertona, M.; Minoretto, P.; Geroldi, D. An open-label trial of L-5-hydroxytryptophan in subjects with romantic stress. *Neuroendocrinol. Lett.* **2010**, *31*, 663.
63. Zavarise, P.; Dalla Volta, G. A Combination of *Tanacetum parthenium*, *Griffonia simplicifolia* and Magnesium (Aurastop) as Symptomatic Acute Treatment for Migraine Aura: A Retrospective Cohort Study. *Open Access Libr. J.* **2017**, *4*, 1–9. [CrossRef]
64. Antonaci, F.; Rebecchi, V.; Sances, G.; Giorgetti, M.P.; Di Palma, F.; Matta, E.; Dalocchio, C.; Tassorelli, C.; Pezzini, A.; Dalla Volta, G. On behalf of the Italian Society for the study of migraine headache (SISC-Lombardia), Italy. AURASTOP® in the treatment of migraine aura. *Int. J. Neurol. Brain Disord.* **2018**, *5*, 11–14.
65. Ferrara, P.; Di Ruscio, F.; Bellomo, A.R.; Ianni, A.; Petitti, T.; Pettoello-Mantovani, M. P507 *Tanacetum parthenium*, *Griffonia simplicifolia* and magnesium as symptomatic and prophylactic treatment for headache in paediatric patients. *Arch. Dis. Child.* **2019**, *104*, A356. [CrossRef]
66. Maletto, P.; Maiullo, D. Composition and Method for Enhancing Neuromuscular Facilitation and Cognitive Functions. 2007. Available online: [https://patentscope.wipo.int/search/pt/detail.jsf?sessionId=96ABE442E361F3563964BFF0917DDF8D.wapp1nA?docId=WO2007127773&\\_cid=P10-KBV2T5-88110-9](https://patentscope.wipo.int/search/pt/detail.jsf?sessionId=96ABE442E361F3563964BFF0917DDF8D.wapp1nA?docId=WO2007127773&_cid=P10-KBV2T5-88110-9) (accessed on 30 October 2021).

67. Mech, G. Protein Dietary Supplement. 2016. Available online: <https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2016046795> (accessed on 30 October 2021).
68. Zuckerman, A. Appetite Suppressant Toothpaste. Available online: [https://patentscope.wipo.int/search/en/detail.jsf?docId=US39887399&\\_fid=US40056806](https://patentscope.wipo.int/search/en/detail.jsf?docId=US39887399&_fid=US40056806) (accessed on 30 October 2021).
69. Alvin, N.; Harriet, N. Dietary Supplement for Suppressing Appetite, Enhancing and Extending Satiety, Improving Glycemic Control, and Stimulant Free. 2006. Available online: [https://patentscope.wipo.int/search/en/detail.jsf?docId=US41535038&\\_cid=P20-KRMB99-59604-1](https://patentscope.wipo.int/search/en/detail.jsf?docId=US41535038&_cid=P20-KRMB99-59604-1) (accessed on 30 October 2021).
70. Lu, X. Medicine for Treating and Adjusting Depression and Products for Preparation of Medicine. 2018. Available online: [https://patentscope.wipo.int/search/en/detail.jsf?docId=CN224403837&\\_cid=P20-KRMBDJ-60911-1](https://patentscope.wipo.int/search/en/detail.jsf?docId=CN224403837&_cid=P20-KRMBDJ-60911-1) (accessed on 30 October 2021).
71. Jain, R.; Jindal, K.C. Composition Comprising at Least one Higher Aliphatic Alcohol and Extract of Griffonia simplicifolia. 2007. Available online: [https://patentscope.wipo.int/search/en/detail.jsf?docId=MY203010636&\\_cid=P20-KRMBSH-64436-1](https://patentscope.wipo.int/search/en/detail.jsf?docId=MY203010636&_cid=P20-KRMBSH-64436-1) (accessed on 30 October 2021).
72. Heyda, A. Compositions for the Treatment of Anxiety and Associated Disorders. European Patent Application No. EP1502597, 2 February 2005.
73. Purificacion, B.Q.; Gabriel, E.G.; Ferran, J.R.; Miquel, J.R. NUTRITIONAL Supplement is for Treatment of Syndromes Related to Fatigue, Including Pain, Muscular Problems, Anxiety, Depression and Periods of Fatigue. 2004. Available online: [https://patentscope.wipo.int/search/en/detail.jsf?docId=ES32025221&\\_cid=P20-KRMBWY-65528-1](https://patentscope.wipo.int/search/en/detail.jsf?docId=ES32025221&_cid=P20-KRMBWY-65528-1) (accessed on 30 October 2021).
74. Yang, C. Nutritional Health-Care Green Bean Eight-Treasure Rice Pudding. 2017. Available online: [https://patentscope.wipo.int/search/en/detail.jsf?docId=CN199372205&\\_cid=P20-KRMC3B-67207-1](https://patentscope.wipo.int/search/en/detail.jsf?docId=CN199372205&_cid=P20-KRMC3B-67207-1) (accessed on 30 October 2021).
75. Dare, P. Liquid Mixture for Electronic Devices. 2013. Available online: <https://worldwide.espacenet.com/patent/search/family/048446562/publication/ITVR20130072A1?q=ITVR20130072A1> (accessed on 30 October 2021).
76. Bertolino, M.F. Integratore Alimentare Coadiuvante Nelle Patologie del Tubo Digerente Anche con Eventuale Componente Ansiosa-Depressiva. 2013. Available online: <https://worldwide.espacenet.com/patent/search/family/046690608/publication/ITPA20120009A1?q=ITPA20120009A1> (accessed on 30 October 2021).
77. Bollen, P.; Chamberland, G.; Devaux, C. Compositions Comprising Plant Extracts and Use Thereof for Treating Inflammation. 2010. Available online: <https://worldwide.espacenet.com/patent/search/family/042072988/publication/CA2736914A1?q=CA2736914A1> (accessed on 30 October 2021).
78. Talbott, S. Nutritional Supplements Affecting Mood State and Sleep Quality. 2021. Available online: <https://worldwide.espacenet.com/patent/search/family/065526093/publication/US2021069282A1?q=US2021069282A1> (accessed on 30 October 2021).
79. Heyda, A. Compositions for Relieving Symptoms of Menopausal Syndrome. 2003. Available online: <https://worldwide.espacenet.com/patent/search/family/011448704/publication/EP1321149A1?q=Compositions%20for%20relieving%20symptoms%20of%20menopausal%20syndrome> (accessed on 30 October 2021).
80. Heuer, M.A.; Gardiner, O.T. Weight Loss Composition and Method of Inducing Weight Loss. 2005. Available online: <https://worldwide.espacenet.com/patent/search/family/035320731/publication/AU2005240125A1?q=AU2005240125A1> (accessed on 30 October 2021).
81. Pialorsi, F.L.; Seneci, A.E. Formulations Comprising Arginine and/or a Pharmaceutically Acceptable Salt Thereof and an Acid Active Ingredient with a PKA of 1–5. 2021. Available online: <https://worldwide.espacenet.com/patent/search/family/069106081/publication/WO2021038486A1?q=WO2021038486A1> (accessed on 30 October 2021).
82. Kowatsch, C.M. Use of e.g., Selective Serotonin Reuptake Inhibitors, Noradrenaline Reuptake Inhibitors, Dopamine Reuptake Inhibitors, and Tricyclic or Tetracyclic Antidepressants to Produce Drugs for the Treatment of Lovesickness. 2010. Available online: <https://worldwide.espacenet.com/patent/search/family/041664419/publication/AT507103A2?q=AT507103A2> (accessed on 30 October 2021).
83. Heyda, A. Equol-Enriched Plant Extract Obtainable by Fermentation. 2006. Available online: <https://worldwide.espacenet.com/patent/search/family/035058248/publication/EP1637609A1?q=EP1637609A1> (accessed on 30 October 2021).
84. Bigliardi, D.; Marangoni, M. Food Composition and Its Use in the Treatment of Sleep Disorders. 2020. Available online: <https://worldwide.espacenet.com/patent/search/family/066286709/publication/IT201900001121A1?q=IT201900001121A1> (accessed on 30 October 2021).
85. Stankov, B.M. Controlled-Release Formulations Containing Tryptophan and/or 5-Hydroxytryptophan. 2006. Available online: <https://worldwide.espacenet.com/patent/search/family/035385157/publication/EP1637185A1?q=EP1637185A1> (accessed on 30 October 2021).
86. Cavallo, G.; Corsini, G.U.; Scarselli, M. Associazione Terapeutica per il Trattamento della Malattia di Parkinson. 2010. Available online: <https://worldwide.espacenet.com/patent/search/family/041349345/publication/ITRM20090299A1?q=ITRM20090299A1> (accessed on 30 October 2021).

87. Cho, S.H.; Perkes, L. Methods and Materials for Treating Depression and Mood Disorder. 2000. Available online: <https://worldwide.espacenet.com/patent/search/family/026790154/publication/US6068846A?q=US6068846A> (accessed on 30 October 2021).
88. Seneci, A. Food and/or Nutraceutical Composition Containing Pea. 2017. Available online: <https://worldwide.espacenet.com/patent/search/family/054843905/publication/EP3130336A1?q=EP3130336A1> (accessed on 30 October 2021).

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.