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RESEARCH ARTICLE

Cost variation analysis of herbal phytoconstituents and nutraceuticals as a neuroprotective in neurodegenerative disorders

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ABSTRACT

Objective: The objective of the study was to find out the cost variation among herbal phytoconstituents and nutraceuticals used for the treatment of neurodegenerative disorders. **Background:** This paper discusses the cost-variation analysis of herbal phytoconstituents and nutraceuticals used as neuroprotective in neurodegenerative disorders. Neurodegenerative disorders are characterized by the loss of nerve cells in the various regions of the brain, which leads to problems such as cognitive impairments and motor problems. Herbal phytoconstituents and nutraceuticals are frequently used for neurodegenerative disorders. The turnover of the Indian herbal industry is more than Rs 80 billion. There are various pharmaceutical companies with innumerable brands, and there is great variability in the price of herbal phytoconstituents and nutraceutical formulations depending on the brand. **Materials and Methods:** The cost variation of various herbal phytoconstituents and nutraceuticals used in neurodegenerative disorders produced by different pharmaceutical companies in India was analyzed. The data was collected by authors from https://amazon.in, https://www.1mg.com, https://kiwla.com, https://netmeds.com, and https://thekiwla.com. **Results:** In India, 15 herbal phytoconstituents and nutraceuticals with 45 formulations under 390 brands produced by various pharmaceutical companies are used as neuroprotective. Among all the herbal phytoconstituents and nutraceuticals, the maximum percentage cost variation and cost ratio were found for Brahmi 500 mg. The minimum percentage cost variation and cost ratio were found for panax ginseng 1000 mg. **Conclusion:** We can conclude that there is a very high-cost variation in the different marketed formulations of herbal phytoconstituents and nutraceuticals used as neuroprotective in neurodegenerative disorders.

KEY WORDS: Amyotrophic lateral sclerosis, Herbal phytoconstituent, Neurodegenerative disorder, Nutraceutical

INTRODUCTION

The gradual loss of neuronal cells is a hallmark of neurodegenerative disorders.[1,2] The fact that neurodegenerative disorders are derived from the unfolding of altered proteins leads to the formation of β structures and a pathological tendency to accumulate in neuronal cells, such as in Parkinson's disease α synuclein protein and in Alzheimer's disease tau protein.[3] Around 15% of people worldwide suffer from neurological disorders, which are the primary cause of both physical and cognitive impairment worldwide.[4] Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis (ALS) are the most common types of neurodegenerative disorders.[5] Parkinson's disease is a long-lasting, progressive neurodegenerative condition manifested by early,

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significant dopaminergic neuron loss in the substantia nigra pars compacta and by the common presence of the intracellular protein α synuclein.[6] Parkinson's disease's hallmark symptoms, such as bradykinesia, tremor, stiffness, and later postural instability, are brought on by a dopamine deficit in the basal ganglia.[7,8] Parkinson's disease is distinguished by mitochondrial dysfunction, an increase in the level of oxidative stress, and a disbalance in dopaminergic neurotransmission.[9] The most common type of dementia, Alzheimer's disease, is distinguished by a progression from episodic memory-related issues to a gradual overall decline in cognitive function.[10,11] The pathology of Alzheimer's disease is characterized by a complex relationship of several biochemical changes, such as modifications in the metabolism of amyloid precursor proteins, oxidative stress, phosphorylation of the tau protein, diminished energetics, inflammation, mitochondrial dysfunction, membrane lipid dysregulation, and disruption of different neurotransmitter signaling pathways.[12] Cortical, brainstem, and spinal anterior horn motor neuron loss is a hallmark of ALS. After Parkinson's and Alzheimer's, it is the third most prevalent type of neurodegenerative disorder.[13] ALS symptoms include progressive muscle weakness, cramping, muscle atrophy, slowness of movement, fasciculation, and stiffness.[14] A severe monogenetic neurodegenerative disorder called Huntington's disease is marked by difficulties with mobility, cognitive impairments, and psychological symptoms.[15] Huntington's disease is brought on by a single huntingtin gene dominant allele with an increased number of CAG repeats.[16,17] The importance of this study is that many people who cannot afford herbal phytoconstituents and nutraceuticals due to their high cost will also be able to buy herbal phytoconstituents and nutraceuticals, which will benefit society. There are various studies that suggest that herbal phytoconstituents and nutraceuticals are utilized for the treatment of neurodegenerative disorders, as summarized in Table 1. A brief description of the herbal phytoconstituents and nutraceuticals used for neurodegenerative disorders is given in Table 2.

Drug therapy for neurodegenerative disorders

Various categories of drugs utilized in the treatment of neurodegenerative disorders produce harmful side effects and adverse drug reactions, which are major drawbacks of the therapy.[18] Donepezil, a cholinesterase inhibitor utilized in the treatment of Alzheimer's disease, has the side effects of insomnia, loss of appetite, and nausea and vomiting.[19] Levodopa is mostly prescribed for Parkinson's patients and has various side effects, including orthostatic hypotension, nausea, and vomiting.[20] Other drugs used for the treatment of neurodegenerative disorders also have side effects and harmful effects. Nutraceuticals and phytoconstituents are currently used most frequently with drug therapy to improve the therapy and also reduce the adverse effects of the drug therapy.[21]

MATERIALS AND METHODS

The cost variation of various herbal phytoconstituents and nutraceuticals used in neurodegenerative disorders produced by different pharmaceutical companies in India was analyzed. The cost of 10 tablet/capsule from various brands was calculated, and a cost variation analysis was done. In this study, the authors analyzed the variation in the cost of different brands of herbal phytoconstituents and nutraceuticals using the data from https://amazon.in, https://www.1mg.com, https://kiwla.com, https://netmeds.com, and https://thekiwla.com. The study was conducted in the month of August 2023.

Table 1: Herbal phytoconstituents and nutraceuticals as a treatment for neurodegenerative disorders

S. No.	Herbal phytoconstituents/Nutraceuticals	Neurodegenerative disorders	References
1.	Brahmi	Alzheimer's disease	[22]
2.	Quercetin	Parkinson's disease	[23]
3.	Ashwagandha	Alzheimer's disease	[24]
4.	Lycopene	Parkinson's disease	[25]
5.	Luteolin	Alzheimer's disease	[26]
6.	Panax ginseng	Alzheimer's disease	[27]
7.	Curcumin	Huntington's disease	[28]
8.	Ginko biloba	Parkinson's disease	[29]
9.	Catechin	Parkinson's disease	[30]
10.	Garlic	Alzheimer's disease	[31]
11.	Omega 3-Fatty acid	Parkinson's disease	[32]
12.	Beta carotene	Parkinson's disease	[33]
13.	L-theanine	Parkinson's disease	[34]
14.	Shankhpushpi	Cognitive impairment	[35]
15.	Coenzyme Q10	Alzheimer's disease	[36]

Table 2: Description of herbal phytoconstituents and nutraceuticals used in neurodegenerative disorders

S. No.	Name	Sources	Description	References
1.	Brahmi	Brahmi consists of the fresh and dried leaves and stem of *Centralla asiatica*	Brahmi is a well-known plant in the huge and rich list of herbs utilized by Ayurveda, and it is widely employed in the treatment of neurological and psychiatric diseases in Ayurveda along with other traditional medical systems. The active ingredients found in brahmi belong to the alkaloids, glycosides, favonoids, and saponins categories.	[37]
2.	Quercetin	Citrus fruits, apples, onions, parsley, sage, tea, and red wine	Quercetin is a member of the flavonoid plant pigment family, which is responsible for the colour of many fruits, flowers, and vegetables. Quercetin is one type of flavonoid that is an antioxidant. They scavenge reactive oxygen species, which are metabolic particles that can harm cell membranes, alter DNA, or even trigger cell death.	[38]
3.	Ashwagandha	Dried root of *Withania somnifera* plant	Ashwagandha reduces the activity of enzymes that cause oxidative stress in the brain, including glutathione, superoxide dismutase, catalase, and lipid peroxidation. Steroidostane-containing steroidal lactones, including sitoindosides, withanone, withaferin, withanolides, and around 0.2% alkaloids, are present in the root extract.	[39]
4.	Lycopene	Red fruits and vegetables such as tomatoes, pink guavas, apricots, watermelons, and pink grapefruits	Lycopene is an aliphatic hydrocarbon carotenoid. Research has demonstrated that through its anti-oxidative, anti-inflammatory, and anti-proliferative properties, lycopene can have both preventive and therapeutic benefits for a variety of illnesses, including neoplasms and heart failure. Lycopene also has preventive and therapeutic effects on a variety of conditions affecting the CNS, including depression, cerebral ischemia, Parkinson's disease, Alzheimer's disease, and Huntington's disease.	[40]
5.	Luteolin	Celery, green pepper, parsley, perilla leaf, and chamomile tea	Among its many benefits are its ability to scavenge free radicals and exhibit anti-inflammatory, antioxidant, anticancer, antibacterial, antiulcer, anti-influenza, cytoprotective, hepatoprotective, neuroprotective, neurotrophic, and neurogenesis activity, cardioprotective, and macrophage polarization effects.	[41]
6.	Panax ginseng	Dried root of *Panax ginseng*	Ginsenosides are the primary active ingredients in Panax ginseng; they are triterpene saponins. The ginseng Panax has anti-diabetic, anti-inflammatory, anti-sterility, anti-cancer, antioxidant, and anti-proliferative properties.	[42]
7.	Curcumin	Rhizome of curcuma longa	Famous Indian spice turmeric, also known as Curcuma longa, has been used for generations in herbal remedies to cure a wide range of conditions, including rheumatism, ulcers caused by diabetes, anorexia, cough, and sinusitis. The primary curcuminoid in turmeric, known as diferruloylmethane, is what gives it its yellow colour. Significant anti-inflammatory, antioxidant, anti-carcinogenic, anti-mutagenic, anticoagulant, and anti-infective properties of curcumin have been reported.	[43]
8.	Ginko biloba	Leaves of Ginko biloba tree	The primary bioactive substances found in G. biloba leaves include flavonoids and terpenoids. The primary bioactive substances in G. biloba are the acids known as phenolic. Current pharmacological research has reported the potential use of crude extracts or compounds derived from G. biloba leaves, seeds, and exocarp in the treatment of a variety of illnesses, including non-alcoholic fatty liver, allergies and asthma, cancer, dementia, coronary artery disease, and cerebrovascular and cardiovascular disorders.	[44]
9.	Catechin	Unfermented green tea	Among the many advantages of catechins is their ability to prevent or lessen skin damage. Tea leaves contain a valuable component called catechins, which have potent antioxidant properties and physiologically significant effects. These belong to the class of chemicals called polyphenols that are present in many therapeutic plants. Seventy-five to eighty percent of green tea leaves are made up of water and polyphenol chemicals (flavanols, flavandiols, flavonoids, and phenolic acid), of which more than 75% are catechins.	[45]

(Contd...)

Table 2: *(Continued)*

S. No.	Name	Sources	Description	References
10.	Garlic	Bulb of the plant *Allium sativum*	One of the spices that is most frequently used in cooking is garlic. Because of its organosulfur components, it has also been employed since the beginning for conventional plant-based therapy. It has been discovered that garlic contains significant biological qualities with great medicinal potential. These qualities depend on how the root is used, prepared, and extracted. It has been said to possess immunomodulatory, anti-inflammatory, and antioxidant properties. Garlic, notably its organosulfur compounds, have beneficial effects on immune cells, particularly in controlling the generation and proliferation of cytokines, which help maintain immune system homeostasis.	[46]
11.	Omega 3-Fatty acid	Fish and other seafood (cold-water fatty fish, such as salmon, and mackerel) Nuts and seeds (such as flaxseed, and walnuts) Plant oils (such as soybean oil, and canola oil)	Nutrition is important for psychological wellness, mental illnesses, and the growth of the brain. Omega-3 fatty acids are well known for their benefits to both mental and physical wellness, with the latter benefiting from them as well. As a result of their involvement in numerous physiological processes linked to neurogenesis, neurotransmission, and neuroinflammation, omega-3 fatty acids are essential for the growth, health, and development of the brain.	[47]
12.	Beta carotene	Carrots, spinach, lettuce, tomatoes, sweet potatoes, broccoli, cantaloupe, and winter squash	The carotenoid component that is abundant in human diets and can be found in all human tissues, including blood, is called β-carotene. Its strong bioactivity makes it a popular choice in medicine as well. It serves as a coloring agent for tablets in the pharmaceutical business and as a bioactive component of creams in the cosmetics sector, shielding skin lesions from oxidation and UV light exposure.	[48]
13.	L-theanine	leaves of *Camellia sinensis*	An amino acid called theanine, which is derived from non-proteins, was extracted from green tea leaves. In addition to reducing stress and enhancing cognitive performance in AD patients, L-theanine has anti-inflammatory and antioxidant qualities. It is also used for the prevention of cardiovascular disorders and cancer.	[49]
14.	Shankhpushpi	Whole plant of *Convolvulus pluricaulis*	In Ayurveda, Shankhpushpi is an important and native herb that is regarded as a blessing from nature. It is a natural medication that improves memory. It revitalizes the nervous system. It is also a natural booster for kids' mental growth. It's a strong, pungent, bitter tonic that enhances the mind, helps with bronchitis, improves complexion, biliousness, epilepsy, and baby teething issues, among other things.	[50]
15.	Coenzyme Q10	CoQ10 is found in meat, fish and nuts.	CoQ10, which is found in mitochondria and the membranes of cells in both reduced and oxidized forms, is a necessary cofactor in the process of oxidative phosphorylation. In addition to being an antioxidant and anti-inflammatory, CoQ10 also has the ability to stop inflammatory signaling pathways from being activated and free radical damage from occurring. Coenzyme Q10 is being used more often in neurodegenerative disorders like HD, AD, and PD.	[51]

In this study author selected the inclusion and exclusion criteria as below:

Inclusion criteria

- Nutraceutical and herbal phytoconstituents sold as such or in their own special formulation were used for neurodegenerative disorders
- Products made by Indian pharmaceutical companies that contained the indicated nutraceuticals and herbal phytoconstituents were utilized
- Nutraceuticals and herbal phytoconstituents that had full product information, such as cost, brand name, strength, and formulations
- To determine the price, the drug's stripes were analyzed
- Only tablet/capsule dosage forms of herbal phytoconstituents and nutraceuticals were included in the study.

Exclusion criteria

- Herbal phytoconstituents and nutraceuticals made by the same industry were not included in this study
- Nutraceuticals and herbal phytoconstituents, other than oral formulations, were excluded from the study
- Nutraceuticals and herbal phytoconstituents that were available in combination with others were also excluded from this study

Table 3: Cost variation analysis of herbal phytoconstituents and nutraceuticals

S. No.	Herbal phytoconstituents and nutraceutical names	No. of Brands	Dosage Form (Tablet/ Capsule)	Strength	Minimum price in Indian Rupees (INR)	Maximum price in Indian Rupees (INR)	Cost ratio	Percentage cost variation (%)
1	Brahmi	15	Tab/Cap	500 (mg)	9	378	42	4100
		2	Tab/Cap	1000 (mg)	58	97	1.67	67.24
2.	Quercetin	8	Tab/Cap	100 (mg)	89	333	3.74	274.15
		9	Tab/Cap	400 (mg)	330	458	1.38	38.78
		11	Tab/Cap	500 (mg)	331	970	2.93	193.05
		5	Tab/Cap	1000 (mg)	299	1050	3.51	251.17
3.	Ashwagandha	9	Tab/Cap	250 (mg)	29	432	14.89	1389.65
		13	Tab/Cap	500 (mg)	50	898	17.96	1696
		7	Tab/Cap	600 (mg)	158	349	2.20	120.88
		12	Tab/Cap	1000 (mg)	25	217	8.68	768
4.	Lycopene	5	Tab/Cap	5 (mg)	66	813	12.31	1131.81
		8	Tab/Cap	10 (mg)	85	788	9.27	827.05
		4	Tab/Cap	15 (mg)	609	2079	3.41	241.37
		6	Tab/Cap	20 (mg)	638	1400	2.19	199.43
		7	Tab/Cap	25 (mg)	110	2067	18.79	1779.09
		4	Tab/Cap	30 (mg)	211	1152	5.45	445.97
5.	Luteolin	4	Tab/Cap	100 (mg)	150	897	5.98	498
		3	Tab/Cap	200 (mg)	188	6750	35.90	3490.42
6.	Panax ginseng	5	Tab/Cap	400 (mg)	101	199	1.97	97.02
		6	Tab/Cap	500 (mg)	80	200	2.5	150
		4	Tab/Cap	600 (mg)	255	785	3.07	207.84
		3	Tab/Cap	1000 (mg)	116	129	1.11	11.20
7.	Curcumin	5	Tab/Cap	500 (mg)	160	749	4.68	368.12
		3	Tab/Cap	600 (mg)	90	245	2.72	172.22
		7	Tab/Cap	1310 (mg)	124	266	2.14	114.51
		9	Tab/Cap	1500 (mg)	167	638	3.82	282.03
8.	Ginko biloba	26	Tab/Cap	120 (mg)	84	564	6.71	571.42
9.	Catechin	12	Tab/Cap	250 (mg)	41	233	5.68	468.29
		5	Tab/Cap	400 (mg)	71	194	2.73	173.23
		23	Tab/Cap	500 (mg)	83	583	7.02	602.40
		19	Tab/Cap	1000 (mg)	106	1442	13.60	1260.37
10.	Garlic	10	Tab/Cap	500 (mg)	55	1433	26.05	2505.45
		6	Tab/Cap	1000 (mg)	229	2467	10.77	977.29
11.	Omega 3-Fatty acid	11	Tab/Cap	500 (mg)	132	233	1.76	76.51
		13	Tab/Cap	1000 (mg)	50	895	17.9	1690
		5	Tab/Cap	1250 (mg)	9	68	7.55	655.55
		8	Tab/Cap	1500 (mg)	91	200	2.19	119.78
12.	Beta carotene	2	Tab/Cap	25000 (IU)	150	243	1.62	62
13.	L theanine	10	Tab/Cap	100 (mg)	156	1329	8.51	751.92
		12	Tab/Cap	200 (mg)	126	500	3.96	296.82
		8	Tab/Cap	250 (mg)	144	961	6.67	567.36
14.	Shankhpushpi	7	Tab/Cap	500 (mg)	65	133	2.04	104.61
15.	Coenzyme Q10	8	Tab/Cap	100 (mg)	166	869	5.23	423.49
		17	Tab/Cap	200 (mg)	195	2341	12	1100.51
		14	Tab/Cap	300 (mg)	416	2199	5.28	428.60

- Inaccurate information on the price, brand name, strength, and formulation of nutraceuticals and herbal phytoconstituents was not included in this study.

In this study, the highest price of the herbal phytoconstituents and nutraceuticals is divided by their lowest price to calculate the cost ratio. The cost percent variation is calculated by the formula given below:

$$Cost\ variation\ (\%) = \frac{Maximum\ price - Minimum\ price \times 100}{Minimum\ price}$$

RESULTS

In India, 15 herbal phytoconstituents and nutraceuticals with 45 formulations under 390 brands are produced by various pharmaceutical companies. According to the result of this study, there are many different brands of nutraceutical and herbal phytoconstituents on the market, and the cost of these nutraceutical and herbal phytoconstituents varies widely. Among all the herbal phytoconstituents and nutraceuticals, the maximum percentage cost variation and cost ratio were found for brahmi 500 mg, which is 4100 and 1:42, followed by luteolin 200 mg (3490.42 and 1:35.90), garlic 500 mg (2505.45 and 1:26.05), and lycopene 25 mg

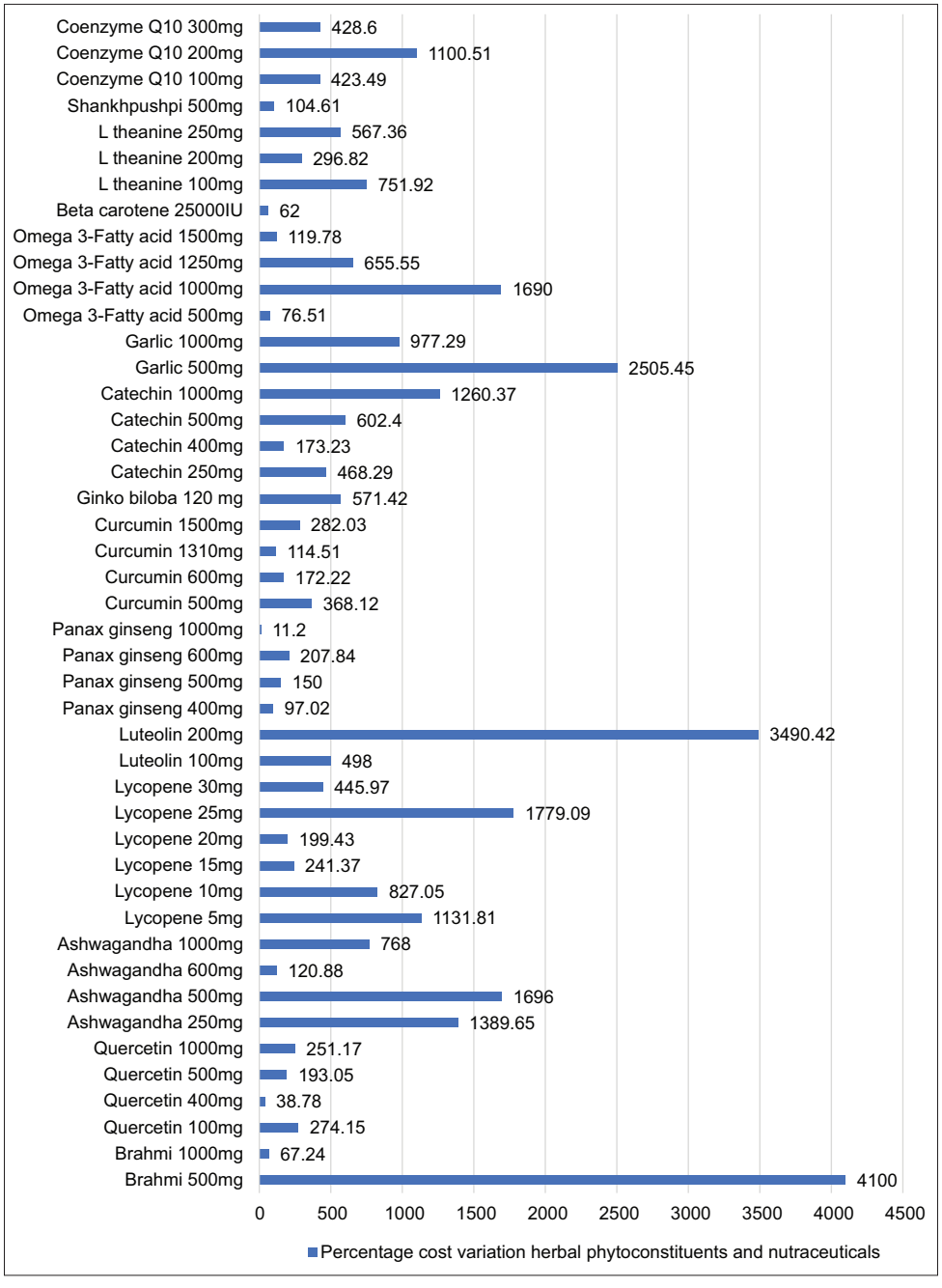

Figure 1: Percentage cost variation analysis of herbal phytoconstituents and nutraceuticals

(1779.09 and 1:18.79). The minimum percentage cost variation and cost ratio were found for panax ginseng 1000 mg, 11.20, and 1:1.1. The maximum number of brands is Ginko biloba 120 mg (26) followed by catechin 500 mg (23), and Coenzyme Q10 200 mg (17). The cost variation of herbal phytoconstituents and nutraceuticals is mentioned in Table 3.

DISCUSSION

Neurodegenerative disorders are a burden to society, and people suffering from these diseases experience lots of problems in their daily routine work. Different herbal phytoconstituents and nutraceuticals are currently more commonly utilized for the prevention and treatment of neurodegenerative disorders. Lycopene, co-enzyme Q10, and curcumin, which are available on the market in different formulations, are most frequently used in Parkinson's disease. Quercetin and luteolin are used in Alzheimer's disease. All these herbal phytoconstituents, such as Brahmi, Ginkgo biloba, and Ashwagandha, are mostly preferred due to their low side effects and beneficial effects on neurodegenerative disorders. The cost variation analysis of various herbal phytoconstituents and nutraceuticals is calculated in this study, and we found that there is a very high variation in the price and that the different brands provide the same formulation at different prices in the Indian market. The highest cost variation was found for Brahmi 500 mg and the lowest for panax ginseng 1000 mg. The cost variation analysis of herbal phytoconstituents and nutraceuticals is shown in Figure 1. Food Safety and Standards Authority of India (FSSAI) is the body that regulates the quality of nutraceuticals and herbal phytoconstituents in India, working in collaboration with the Ministry of Ayush. The prices of herbal phytoconstituents and nutraceuticals are collected using an online website instead of the offline market price, which was the limitation of the study. Hence, it is very important not only for the government but also for health service providers and common people to follow rules and regulations strictly so that we can limit the cost variations in the cost of herbal phytoconstituents and nutraceuticals, thus lowering the price so that everyone can afford it.

CONCLUSION

After conducting this study's analysis, we came to the conclusion that there are several brand names of herbal phytoconstituents and nutraceuticals that exist in the Indian market, along with a wide variation in prices. Among all 15 herbal phytoconstituents and nutraceuticals included in the study, the maximum percentage cost variation and cost ratio were found for Brahmi 500 mg. The minimum percentage cost variation and cost ratio were found for panax ginseng 1000 mg. These herbal phytoconstituents and nutraceuticals are currently used in neurodegenerative disorders, mostly because they have very few adverse effects and due to their beneficial effects. In addition, choosing brands with a low maximum retail price will be economically advantageous. This study is a valuable pharmacoeconomic tool that may assist in lowering the price of disease treatment for patients. The important aspect of this study is that patients will be able to choose low-cost herbal phytoconstituents and nutraceuticals so that the lower middle-class population can afford these products easily. Regulation of the cost of herbal phytoconstituents and nutraceuticals is very necessary to control the variation in their cost. On behalf of our study, we can suggest to policymakers that they should create any regulatory body that controls the cost of herbal phytoconstituents and nutraceuticals. Health-care practitioners should give complete information on the cost variation of herbal phytoconstituents and nutraceuticals to patients so that the majority of the population takes the product at the lowest cost.

Limitation

The cost of the herbal phytoconstituents and nutraceuticals is collected using an online website instead of the offline market price, which was the limitation of the study.

AUTHOR CONTRIBUTIONS

Shashikesh Shukla, Ashutosh Ranjan, and Dr. Shamsher Singh conceptualized and designed the whole manuscript and also conducted the acquisition and interpretation of data. Dr. Shamsher Singh revised the manuscript critically.

ETHICAL APPROVAL

This study is a meta-analysis type of study, and it does not involve any humans or experimental animals, so we do not need any ethical approval for the study.

Guidelines

There are various guidelines for the administration of herbal phytoconstituents and nutraceuticals provided by the USFDA and FSSAI.

USFDA- Dietary Supplements Guidance Documents & Regulatory Information | FDA

FSSAI- 6243ef28079ceDirection_Nutra_30_03_2022.pdf (fssai.gov.in)

DECLARATION OF INTEREST

The statement of declaration by the author is that they have no financial or economic interest or any kind of personal relationship that can appear to influence the reported work in this paper.

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