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Assessment of knowledge about Nutraceutical Regulations and practices among Nutraceutical manufacturer and Pharmacies

Farheen Qamar*[,a], Tabinda Razzaq [b], Syeda Muzammil Kainat [c], Muhammad Nabeel [d]

[a]*Institute of Pharmaceutical Sciences Peoples University of Medical and Health Sciences for Women (PUMHSW) Nawabshah, Pakistan*

[b]*Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences, Lahore, Pakistan.*

[c]*Institute of Pharmaceutical Sciences, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan.*

[d]*Department Clinical Oncology Pharmacy, Cancer Care Hospital & Research Centre, Lahore, Pakistan*.

Abstract

Introduction: The Pakistani nutraceutical industry faces challenges in regulating its products due to insufficient knowledge among manufacturers and pharmacies, despite the Drug Regulatory Authority of Pakistan's 2014 regulations.

Objective: This study aims to assess the level of knowledge and practices regarding nutraceutical regulations among nutraceutical manufacturers and pharmacies in Pakistan. It explores the impact of regulatory practices on the manufacturing, sale, and quality of nutraceutical products.

Materials & Methods: A cross-sectional study was conducted involving 20 nutraceutical manufacturing units across Pakistan and 100 pharmacies and medical stores located in Lahore. Data were collected through a combination of online questionnaires and in-person interviews.

Results: 71.4% of nutraceutical manufacturers in Lahore demonstrated knowledge about the basic definition of nutraceuticals.92.9% of manufacturers in Lahore were aware of the purpose of SRO 412, which regulates herbal, Unani, homeopathic, and nutraceutical products. 64.3% of manufacturers in Lahore understood the significance of product stability during shelf life, while this knowledge was 100% in Peshawar and Islamabad. 90.4% of pharmacies had a pharmacist present, whereas 33.3% of medical stores did not have a pharmacist.74.1% of the pharmacies required prescriptions for nutraceutical sales when pharmacists were present, but only 27.4% of medical stores required prescriptions when pharmacists were absent.

Discussion: The findings highlight the gaps in regulatory knowledge and staff qualifications in the nutraceutical industry, which could compromise product safety and efficacy. Although some regulations are in place, enforcement and education are key issues. The absence of pharmacists in certain settings further complicates compliance with regulations, especially regarding product safety and labelling.

Conclusion: The study underscores the need for improved regulatory education and enforcement in Pakistan's nutraceutical sector. Enhanced training for manufacturers and pharmacies, coupled with stronger regulatory support from DRAP, is essential to ensure the safety and quality of nutraceutical products in the market.

Keywords: Nutraceutical regulations, DRAP, pharmacist involvement, community pharmacies, manufacturing compliance, labelling rules

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*Corresponding author

1. Introduction

The field of nutraceuticals, which combines the terms "nutrition" and "pharmaceuticals," refers to food products that provide health and medical benefits, including the prevention and treatment of disease. The term was first coined in 1989 by Dr. Stephen DeFelice, the Foundation for Innovation in Medicine Chairman, to describe this rapidly growing area of biomedical research(1). Nutraceuticals encompass a broad range of products, including dietary supplements, herbal products, and fortified foods, used globally for their perceived health benefits(2). The concept is rooted in the ancient practice of using natural substances for health and healing, as evidenced by Chinese herbal medicines dating back to

2800 BC, detailed in the Shen Nong Ben Cao Jing (The Herbal Classic of Divine Plowman)(3).

Globally, the regulation of nutraceuticals varies significantly across countries. In India, nutraceutical regulations are outlined in Chapter IV of the New Food Safety and Standard Act of 2006, while in Canada, the Food and Drug Regulation governs these products (4), Pakistan despite being one of the leading producers and consumers of nutraceuticals, has faced challenges in the effective regulation of these products due to the complex nature of alternative medicines and a lack of appropriate evaluation methods(5). The Drug Regulatory Authority of Pakistan (DRAP) introduced specific regulations in 2014 through SRO 412, aimed at overseeing the production and sale of nutraceuticals, herbal, Unani, and homeopathic products. However, the implementation of these regulations has been problematic, with issues such as poor knowledge among manufacturers and inadequate enforcement mechanisms(6).

The challenges in Pakistan's regulatory framework are compounded by a high prevalence of alternative medicine usage, particularly in rural areas with limited access to conventional medical services. Factors such as low literacy rates, socioeconomic barriers, and cultural preferences drive the population to seek health solutions from herbalists, Hakeems, and other non-conventional practitioners(7). Despite the regulations, there is evidence that many nutraceutical products are sold without proper oversight, with pharmacists often absent from the manufacturing units. This raises concerns about the safety, efficacy, and quality control of these products, as well as public awareness and understanding of the associated regulations(8).

This study aims to assess the level of knowledge about nutraceutical regulations and practices among nutraceutical manufacturers and pharmacies in Pakistan. It seeks to identify the gaps in awareness and compliance that hinder the effective regulation of these products. By exploring the perspectives of industry stakeholders, the research will provide insights into the current state of nutraceutical regulation in Pakistan and suggest areas for improvement in policy implementation and industry education. This is particularly critical given the growing market for nutraceuticals and the potential health risks associated with their misuse or poor quality control(9).

2. Materials & Methods

2.1 Ethical Approval

The study's ethics approval was sought from the Ethical Committee of the University College of Pharmacy, University of the Punjab (Reference #: EC/UCP/092/2023). The Hospital Committee of Ethics on Human Research also reviewed and endorsed the study's ethical considerations. Moreover, informed consent was also obtained from all the participants.

2.2 Study Design

The study design was cross-sectional and conducted over six months, from November 2023 to April 2024, to investigate the awareness of nutraceutical regulations and practices among manufacturers and pharmacists. This study was done in different pharmacies (n=17) and medical stores (n=10) in Lahore and nutraceuticals (35) all over Pakistan. The questionnaire consisted of two portions, i.e., one for nutraceutical manufacturers, including manufacturer's basic information, the general orientation of nutraceutical regulations, and DRAP facilitation, and the other for pharmacies and medical stores, including sales, storage, maintenance, and labelling of nutraceutical products at the pharmacies and medical stores.

2.3 Data Collection

A self-structured Questionnaire validated by three independent experts with a Cronbach alpha 0.7 was administered. Data was collected by a team of students pursuing Pharm D who had proper knowledge about data collection and nutraceutical regulations. The data collection process involved two main methods which are personal interviews and online questionnaires. Field executives conducted in-person interviews with the owners of medical stores and pharmacies, ensuring accurate and detailed responses. For the nutraceutical industry sector, a questionnaire was constructed using Google Forms and filled out online by the production managers of the companies. The questionnaire assessed the manufacturer's basic information, including the owner’s qualification, the number of pharmacists, the production in charge’s qualification, market coverage, and the area available in the manufacturing unit. This questionnaire evaluated the general orientation of nutraceutical regulations, knowledge about rules, and DRAP facilitation of the nutraceutical manufacturers. The second part of the questionnaire was for community pharmacies and medical stores, and it evaluated the availability of alternative products, their sale, the product’s specifications, and labelling, and the purchasing requirements of nutraceutical products, such as from which manufacturer to buy and which are essential documents that are required.

2.4 Study Population

The study population consisted of 84 pharmacies in Lahore, 16 medical stores, and 35 nutraceutical industries nationwide. Lahore was divided into five convenient zones: north, south, east, west, and centre. Approximately 17 pharmacies and 3 medical stores were selected for data collection in each zone. These medical stores and pharmacies were selected based on their proximity to hospitals, ensuring a diverse and representative sample. In the nutraceutical sector, 35 industries were approached for data collection, but only 20 complete responses were received and considered in the final analysis.

2.5 Inclusion Criteria

The study included pharmacies, medical stores, and nutraceutical industries willing to participate and provide information regarding their practices and awareness of nutraceutical regulations. The inclusion criteria ensured that the participants had a relevant background and experience in dealing with nutraceutical products, making their responses valuable for the study's objectives.

2.6 Exclusion Criteria

Incomplete responses were excluded from the study. Out of 35 nutraceutical industries, only 20 provided complete responses, whereas, 10 incomplete responses were excluded from the analysis. The exclusion criteria ensured that only reliable and comprehensive data were used in the study, enhancing the validity of the findings.

2.7 Data Analysis

The collected data were analysed using SPSS version 26 (Statistical Program for Social Sciences). Cross-tabulation for the frequency distribution of all categorical variables was conducted to understand the distribution of responses. The chi-square test was used to determine associations between variables, with a P value of ≤0.05 considered statistically significant.

3. Result:

3.1 Section 1: Industry data

The survey collected data from 20 nutraceuticals across Pakistan. The respondents were categorized based on cities, indicating that 14 were from Lahore, 1 from Islamabad, 2 from Faisalabad, 2 from Karachi, and 1 from Peshawar.

3.2 Manufacture's Basic Characteristics

Regarding the educational qualification of the nutraceutical manufacturers, the results revealed that in Lahore, 64.3% of the owners possessed a Master's degree. In Islamabad, 100% had an MBA degree, and in Peshawar, 100% were BSc graduates. It was disappointing that most nutraceutical industries employed less than 7 pharmacists in the manufacturing plant. Concerning the qualification of production supervisors, it was surprising that the majority had a master's degree, despite the regulatory authority's DRAP's rule that qualified pharmacists must supervise the production of nutraceuticals.

According to the target consumer profile findings, 85.7% of Lahore manufacturers have local market coverage, while in Islamabad, Karachi, and Peshawar it was 100%. The results also indicated that Out of 14 companies based in Lahore 78.6 mostly prepared solid and liquid dosage forms including (tablets, capsules, syrups, and suspensions). (Table 1).

Table 1. Manufacturer's Basic Information

Parameters	Lahore (n=14)	Islamabad (n=1)	Faisalabad (n=2)	Karachi (n=2)	Peshawar (n=1)	p-values
Owner's Qualification						
Master	9(64.3%)	0	1(50%)	1(50%)	0	0.160
BSC	3(21.4%)	0	0	0	1(100%)	
MBA	1(7.1%)	1(100%)	1(50%)	0	0	
M.Phil.	1(7.1%)	0	0	1(50%)	0	
No. of pharmacist						
>7	3(21.4%)	1(100%)	0	1(50%)	0	0.496
<7	4(28.6%)	0	1(50%)	0	1(100%)	
No pharmacist	7(50%)	0	1(50%)	1(50%)	0	
Production In-charge Qualification						
Masters	1(7.1%)	1(100%)	0	0	0	0.072
B.pharm	4(28.6%)	0	0	1(50%)	0	
Pharm D	0	0	1(50%)	0	1(100%)	
BSc	8(57.1%)	0	1(50%)	1(50%)	0	
Nil	1(7.1%)	0	0	0	0	
Market Coverage						
Local	12(85.7%)	1(100%)	2(100%)	1(50%)	1(100%)	0.806
International	1(7.1%)	0	0	1(50%)	0	
Area available in Manufacturing unit						
Tablet	2(14.3%)	0	0	0	0	0.992
Capsule	1(7.1%)	0	0	0	0	
Any other	11(78.6%)	1(100%)	2(100%)	2(100%)	1(100%)	

3.3 Knowledge Regarding Nutraceuticals Regulation

Knowledge of nutraceutical regulations was assessed using a questionnaire aimed to ascertain the knowledge about the current guideline, as outlined in Table 2. The survey revealed varying levels of understanding among industry professionals in different regions, In Lahore 71.4%, 100% in Faisalabad, 50% in Karachi, and 100% in Peshawar demonstrated awareness of the basic definition of nutraceutical with a significant P value (0.005). It was quite disheartening that industrial employees in Islamabad (100%) and Peshawar (100%) did not know that DRAP was established in 2012.

On the other hand, most of the industries in Lahore (92.9%), Faisalabad (50%), Karachi, and Peshawar (100%) were well aware that SRO stands for statutory reconciliation order. Indicating a good understanding of the purpose of SRO with a significant P value (0.001). In terms of form usage, Industries in Lahore (100%), Faisalabad (100%), Karachi (100%), and Peshawar (100%), had sufficient knowledge that Form 1 is used for the application of local manufacturers, Form 3 for enlistment of locally manufactured alternative medicines and that Form 2 for enlistment as an importer with significant P value (0.001). Furthermore, all respondents

from Lahore, Faisalabad, Karachi, and Peshawar were familiar that a local nutraceutical manufacturer is enlisted by DRAP on form 6, except for Islamabad which showed a poor response. All respondents from Lahore, Faisalabad, Karachi, and Peshawar (100%) were cognisant that product enlistment by DRAP is given on form 7. Conversely, respondents from Islamabad (100%) had a lack of awareness in this area.

Table 2. General Orientation of Nutraceutical Regulations

Question	Lahore (n=14)	Islamabad (n=1)	Faisalabad (n=2)	Karachi (n=2)	Peshawar (n=1)	p-value
What are Nutraceuticals?						
The multi-ingredient substance of natural origin	10(71.4%)	-	2(100%)	1(50%)	1(100%)	
Single entity molecule of synthetic origin	-	1(100%)	-	-	-	0.005*
One or more drug subs derived from plants	4 (28.6%)	-	-	1(50%)	-	
In which year DRAP was formed?						
1976	3(21.4%)	1(100%)	1(50%)	-	1(100%)	0.172
2012	11(78.6)	-	1(50%)	2(100%)	-	
SRO stand for?						
Statutory reconciliation order	13(92.9%)	-	1(50%)	2(100%)	1(100%)	0.066
Service rule order	1(7.1%)	1(100%)	1(50%)	-	-	
What was the purpose of SRO 412?						
To regulate herbal, Unani, homeopathic, nutraceutical	14(100%)	-	2(100%)	2(100%)	1(100%)	0.000
To regulate narcotic	-	1(100%)	-	-	-	
SRO 412 is specifically aimed for?						
Herbal and	1 (7.1%)	-	-	-	-	0.978
nutraceutical	-	-	-	-	-	
Unani	-	-	-	-	-	
Homeopathic	13(92.9%)	1(100%)	2(100%)	2(100%)	1(100%)	
All of above						
Which form is used for application of local manufacturers of nutraceuticals?						0.000
Form 1	14(100%)	-	2(100%)	2(100%)	1(100%)	
Form 2	-	-	-	-	-	
Form 3	-	1(100%)	-	-	-	
Which form is used for enlistment of locally manufactured alternative medicines?						0.896
Form 1	1(7.1%)	-	1(50%)	-	-	
Form 2	3(21.4%)	-	-	1(50%)	-	
Form 3	9(64.3%)	1(100%)	1(50%)	1(50%)	1(100%)	
Form 4	1(7.1%)	-	-	-	-	

Which form is used for enlistment as importers? **Form 1** **Form 2** **Form 3**	 1(7.1%) 11(78.6%) 2(14.3%)	 - 1(100%) -	 - 2(100%) -	 - 2(100%) -	 - 1(100%) -	0.992
A local nutraceutical manufacturer is enlisted by DRAP on which form? **Form 6** **Form 7**	 14(100%) -	 - 1(100%)	 2(100%) -	 2(100%) -	 1(100%) -	0.000
Product enlistment is given by DRAP on which form? **Form 6** **Form7**	 - 14(100%)	 1(100%) -	 - 2(100%)	 - 2(100%)	 - 1(00%)	0.000

3.4 Knowledge About Regulation

The survey results showed that the majority of respondents from Lahore, Islamabad, Karachi, Peshawar, and Faisalabad knew that a nutraceutical manufacturer must be registered on form 6. When asked whether both enlistment and registration are interchangeable terms, in Islamabad the response rate was perfect at 100% followed by Peshawar (100%), whereas Faisalabad and Karachi stood at (50%), and Lahore at (57.1%). It was encouraging that a significant number of industries identified the correct answer about the enlistment of nutraceuticals on Form 7.

In regards to the Information that a provisional certificate of (GMP) is essential for nutraceutical manufacturing, all respondents provided satisfactory answers. In Lahore, 35.7%, Islamabad 100%, Faisalabad 50%, Karachi 50%, and Peshawar 100% of the industries demonstrated varying levels of awareness that reference standards were not mandatory to be followed in nutraceutical manufacturing. Concerning the stability of nutraceutical dosage forms, the response from Lahore (64.3%) was quite satisfying while Peshawar (100%) and Islamabad (100%) were completely disappointing, Respondents in Lahore (35.7%), Faisalabad (50%), and Karachi (100%) correctly acknowledged that specific therapeutic effects can be claimed for any nutraceutical, whereas industries in Islamabad (100%), Peshawar (100%), Lahore (64.3%), and Faisalabad (50%) lacked awareness on this subject.

Response about the nature of the substance should be mentioned on the pack of any nutraceutical dosage form given correctly by all respondents. Respondents from Lahore (85.7%), Faisalabad (50%), and Peshawar (100%) gave appropriate answers that nutraceuticals couldn't be claimed of any disease modification effect. The majority of respondents also correctly emphasized that the label claims should include contraindications related to pregnancy, lactation, and geriatrics.

Table 3. Knowledge about regulations

Question	Lahore (n=14)	Islamabad (n=1)	Faisalabad (n=2)	Karachi (n=2)	Peshawar (n=1)	p-value
Nutraceutical manufacturer is registered on form 6. **Correct** **Incorrect**	 14(10%) -	 1(100%) -	 1(50%) -	 2(100%) -	 1(100%) -	0.050
Enlistment and registration are the same things. **Correct** **Incorrect**	 8(57.1) 6(42.9%)	 1(100%) -	 1(50%) 1(50%)	 1(50%) 1(50%)	 1(100%) -	0.818
Enlistment of nutraceuticals is given on form 7. **Correct** **Incorrect**	 13(92.9%) 1(7.1%)	 1(100%) -	 2(100%) -	 1(50%) 1(50%)	 1(100%) -	0.389

Provisional certificate (GMP) Is essential for nutraceutical manufacturing. **Correct** **Incorrect**	8(57.1%) 6(42.9%)	1(100%) -	1(50%) 1(50%)	2(100%) -	1(100%) -	0.604
Reference standard is not mandatory to be followed in nutraceutical manufacturing. **Correct** **Incorrect**	5(35.7%) 9(64.3%)	- 1(100%)	1(50%) 1(50%)	1(50%) 1(50%)	1(100%) -	0.655
Stability of nutraceutical dosage form is not essential to be justified during shelf life, **Correct** **Incorrect**	9(64.3%) 5(35.7%)	- 1(100%)	1(50%) 1(50%)	1(50%) 1(50%)	- 1(100%)	0.562
Any nutraceutical can be claimed for a particular therapeutic effect. **Correct** **Incorrect**	5(35.7%) 9(64.3%)	- 1(100%)	1(50%) 1(50%)	2(100%) -	- 1(100%)	0.340
Pack of any nutraceutical must mention the nature of substance on label. **Correct** **Incorrect**	14(100%) -	- 1(100%)	2(100%) -	2(100%) -	1(100%) -	0.000
Nutraceuticals can't be claimed of any disease modification effect. **Correct** **Incorrect**	12(85.7%) 2(14.3%)	- 1(100%)	1(50%) 1(50%)	- 2(100%)	1(100%) -	0.051
Label claim must also mention contraindications related to pregnancy, lactation, and geriatrics. **Correct** **Incorrect**	13(92.9%) 1(7.1%)	1(100%) -	2(100%) -	1(50%) 1(50%)	1(100%) -	0.389

3.5 DRAP Facilitation

Respondents from various cities expressed different opinions on several aspects related to DRAP and nutraceutical manufacturing. Regarding the ease of obtaining company enlistment from DRAP on Form 6, there was a strong disagreement among respondents from Lahore (71.4%) who found it challenging. In comparison, those from Islamabad (100%) and Faisalabad (50%) said getting approval was easy. Moreover, the majority of respondents from Lahore (100%), Faisalabad (50%), and Peshawar (100%) disagreed that DRAP's attitude towards nutraceutical manufacturers was facilitating.

Regarding DRAP's current understanding of nutraceuticals, all respondents from Lahore 64.3%, Faisalabad 50%, Karachi 50%, and Peshawar 100% disagreed that the existing knowledge of nutraceuticals was adequate. There was a diversity of opinions regarding the availability of Reference standards for product enlistment. i.e. Lahore14.3%, Islamabad100%, Faisalabad 50%, and Karachi 50% agreed with the statement, while respondents from Lahore 28.6%, Karachi 50%, Faisalabad 50% and Peshawar 100% disagreed with the notion.

Regarding GMP compliance, a significant number of participants found it easy to adhere to for nutraceutical units, Lahore 28.6%, Islamabad 100%, Karachi 50%, and Peshawar 100%. Many participants from Lahore 35.7%, Faisalabad 50%, Karachi 50%, and Peshawar 100% agreed that enlistment for a nutraceutical product could be achieved by mentioning innovation if a monograph is unavailable. There was a general agreement of respondents

from Lahore 57.1%, and Islamabad 100%, that the API source for nutraceutical manufacturing must comply with GMP standards.

In addition to the knowledge regarding direct contact of primary packaging material with the product, a substantial agreement was observed among respondents from Lahore 64.3%, Faisalabad 50%, Karachi 50%, and Peshawar 100%. Concerning labelling rules for herbal and nutraceutical products that require stability, in this respect, there was general agreement from respondents, and 35.7% of Lahore,100% of Islamabad, and 50% of Karachi-based companies were neutral. The draft of DRAP labelling rule 2016-17 defines all essential labelling requirements of dosage form,71.4% of companies in Lahore, 100% of Faisalabad,100% of Karachi and 100% of Peshawar agreed to the fact, Conversely, all Islamabad-based companies disagreed, while 28.6% of Lahore-based industries remained neutral on this matter.

Table 4. DRAP Facilitation

Question	Lahore (n=14)	Islamabad (n=1)	Faisalabad (n=2)	Karachi (n=2)	Peshawar (n=1)	p-value
Getting enlistment of company from DRAP on form 6 is an easy task. **Agree** **Disagree** **Neutral**	 2(14.3%) 10(71.4%) 2(14.3%)	 - 1(100%) -	 - 1(50%) 1(50%)	 - - 2(100%)	 1(100%) - -	0.079
DRAP's attitude towards nutraceutical manufacturers is facilitating. **Agree** **Disagree** **Neutral**	 - 7(50%) 7(50%)	 - 1(100%) -	 - 1(50%) 1(50%)	 - - 2(100%)	 - 1(100%) -	0.406
DRAP's current understanding towards nutraceutical is sufficient and supportive. **Agree** **Disagree** **Neutral**	 - 5(35.7%) 9(64.3%)	 1(100%) - -	 1(50%) - 1(50%)	 - 1(50%) 1(50%)	 - - 1(100%)	0.049
Reference standards for product enlistment are easily available for product enlistment. **Agree** **Disagree** **Neutral**	 2(14.3%) 4(28.6%) 8(57.1%)	 1(100%) - -	 1(50%) 1(50%) -	 1(50%) 1(50%) -	 - 1(100%) -	0.298
GMP compliance is easy to follow for nutraceutical units. **Agree** **Disagree** **Neutral**	 4(28.6%) 4(28.6%) 6(42.9%)	 1(100%) - -	 - - 2(100%)	 1(50%) - 1(50%)	 1(100%) - -	0.495
For a nutraceutical product whose monograph is unavailable, its enlistment can be achieved by mentioning innovation. **Agree** **Disagree** **Neutral**	 5(35.7%) 4(28.6%) 5(35.7%)	 - 1(100%) -	 1(50%) 1(50%) -	 1(50%) - 1(50%)	 1(100%) - -	0.659
Source of API for nutraceutical manufacturing has to be of GMP standard. **Agree** **Disagree** **Neutral**	 8(57.1%) 1(7.1%) 5(35.7%)	 1(100%) - -	 2(100%) - -	 2(100%) - -	 1(100%) - -	0.885
Primary packaging materials are those parts of drug container which are in direct contact with product. **Agree** **Disagree** **Neutral**	 9(64.3%) 2(14.3%) 3(21.4%)	 - - 1(100%)	 1(50%) 1(50%) -	 1(50%) - 1(50%)	 1(100%) - -	0.560

Herbal drug dosage form does not require any stability criteria, once formulated is stable for the rest of life. **Agree** **Disagree** **Neutral**	 3(21.4%) 6(42.9%) 5(35.7%)	 - - 1(100%)	 1(50%) 1(50%) -	 - 1(50%) 1(50%)	 - 1(100%) -	0.729
The draft of labelling rules 2016-17 DRAP defines all essential labelling requirements to be put on a dosage form. **Agree** **Disagree** **Neutral**	 10(71.4%) - 4(28.6%)	 - 1(100%) -	 2(100%) - -	 2(100%) - -	 1(100%) - -	0.005

3.6 Section 2: pharmacy and medical store data

A total of 84 pharmacies and 16 medical stores participated in the study. The respondents from pharmacies were pharmacists (90.4%), with a smaller number of non-pharmacists (6.7%). Interestingly, a significant proportion of medical stores (33.4%) did not have a pharmacist present, a finding supported by a notable p-value of 0.014. Furthermore, it was appraisable to know that most nutritional supplements like food supplements (54.8%), and vitamins (89%) were predominantly sold under pharmacist supervision. Conversely, sales of herbal (68.5%), Unani (86.3%), and Ayurveda (94.5%) products were highest when pharmacists were absent. However, the sale of nutraceuticals (63%) was maximum. Regarding price range, approximately all the nutraceuticals collocate in the extravagant category (74.1%).

The products were from two main companies' Hamdard (13.7%) and Qarshi (37%). The practice of ensuring prescriptions by authorized personnel was more common in places where pharmacists were present (74.1%), whereas, there was more drift towards self-medication at places lacking pharmacists (27.4%). The pharmacists generally exhibited positive responses about regulations of nutraceuticals set by DRAP. They emphasized the importance of enlistment numbers on the pack of nutraceutical products (78.1%) and insurance of ingredients and strength (84.9%). On the other hand, non-pharmacists showed a lack of knowledge and interest in DRAP's labelling regulations (44.4%). A statistically significant relation was found between knowledge and attitude (p=0.004).

Pharmacists were well cognizant of the discrepancy between the labels of pharmaceutical products and nutraceutical products (64.4%). They also demonstrated efficient knowledge concerning Insurance of the direction of use on the pack (79.5%) and storage conditions (89%). It was quite satisfactory that pharmacists (91.8%), and non-pharmacists (92.6%), were well-informed regarding distributor's warranties and authorization. However, a majority of non-pharmacists (66.7%) expressed that drug inspectors did not typically inspect or sample nutraceutical products.

Table 5. Pharmacy and Medical store data

parameter	Pharmacist available	Pharmacist not available	Probability
Category **A** **B**	 66(90.4%) 7 (9.6%)	 18 (66.7%) 9(33.3%)	0.014
Food supplement **Available** **Not available**	 40 (54.8%) 18 (66.7%)	 33 (45.2%) 9 (33.3%)	0.201
Vitamins **Available** **Not available**	 65 (89%) 24 (88.9%)	 8 (11%) 3 (11.1%)	0.616
Herbal **Available** **Not available**	 23 (31.5%) 12 (44.4%)	 50 (68.5%) 15 (55.6%)	0.166
Unani **Available** **Not available**	 10 (13.7%) 3 (11.1%)	 63 (86.3%) 24 (88.9%)	0.513
Ayurveda **Available** **Not available**	 4 (5.5%) 2 (7.4%)	 69(94.5%) 25(92.6%)	0.517
Top-selling alternative product. **Food supplement and nutraceutical** **Food supplement**	 11 (15.1%) 13 (17.8%)	 5(18.5%) 5 (18.5%)	0.977

Nutraceuticals **Herbal**	46 (63.0%) 3 (4.1%)	16 (59.3) 1 (3.7%)	
Price range **Expensive** **Normal** **Cheap** **All**	 40 (54.8%) 16 (21.9%) 2(2.7%) 15(20.5%)	 20 (74.1%) 24 (14.8%) 0 3 (11.1%)	0.330
Companies of which you have products. **Hamdard** **Qarshi** **Any other** **Hamdard and qarshi**	 7(9.6%) 20(27.4%) 1(1.4%) 45(61.6%)	 4(14.8%) 7(25.9%) 0 16(59.3%)	0.827
Which company occupies most of shelves. **Hamdard** **Qarshi** **Any other** **Hamdard and qarshi**	 10 (13.7%) 27(37.0%) 1(1.4%) 35(47.9%)	 6 (22.2%) 10(37.0%) 0 11(40.7%)	0.685
Most of the prescriptions are from. **Doctor** **Hakeem** **Dispenser** **Pharmacist** **Self-generated**	 40 (54.8%) 2(2.7%) 1(1.4%) 10(13.7%) 20(27.4%)	 20 (74.1%) 1(3.7%) 0 0 6(22.2%)	0.235
Insurance of enlistment no: on pack. **Correct** **incorrect**	 57(78.1%) 16(21.9%)	 18(66.7%) 9(33.3%)	0.180
Insurance that products label has ingredient and strength. **Correct** **incorrect**	 62(84.9%) 11(15.1%)	 22(81.5%) 5(18.5%)	0.443
Are u well acquainted with labelling rules of DRAP. **Correct** **incorrect**	 55(75.3%) 18(24.7%)	 12(44.4%) 15(55.6%)	0.004
Drug inspector inquired about nutraceutical products. **Correct** **incorrect**	 52(71.2%) 21(28.8%)	 18(66.7%) 9(33.3%)	0.416
Label of pharmaceutical or alternative medicines is differentiable. **Correct** **incorrect**	 47(64.4%) 25(34.2%)	 16(59.3%) 11(40.7%)	0.711
Insurance of direction of use on pack. **Correct** **incorrect**	 58(79.5%) 15(20.5%)	 19(70.4%) 8(29.6%)	0.242
Insurance of pack size and expiry date. **Correct** **incorrect**	 69(94.5%) 4(5.5%)	 26(96.3%) 1(3.7%)	0.590
Insurance that label contain storage conditions. **Correct** **incorrect**	 65(89%) 8(11%)	 22(81.5%) 5(18.5%)	0.247
Do you ensure prescription for alternative medicine? **Correct** **incorrect**	 43(58.9%) 30(41.1%)	 19(70.4%) 8(29.6%)	0.208

Insurance of proper warranty from distributor. **Correct** **Incorrect**	 67(91.8%) 6(8.2%)	 25(92.6%) 2(7.4%)	0.630
Is your distributor an authorised agent of manufacturer? **Correct** **incorrect**	 68(93.2%) 5(6.8%)	 23(85.2%) 4(14.8%)	0.196
Authority and warranty of selling agent is insignificant and irrelevant **Correct** **incorrect**	 29(39.7%) 44(60.3%)	 18(66.7%) 9(33.3%)	0.015
Drug inspector collect nutraceutical samples. **Correct** **incorrect**	 30(41.1%) 43(58.9%)	 9(33.3%) 18(66.7%)	0.320

4. Discussion

Nutraceutical products are considered food supplements and have been demonstrated to promote general well-being, help control symptoms, and prevent some common diseases. Over the past year, nutraceuticals have received potential interest among populations due to increased life expectancy, delayed aging, and nutritional support, raising global demand. The nutraceutical industry is evolving day by day in Pakistan and other countries with high manufacturing posing a risk to consumer health. There is a need for global harmonization in the regulatory market for nutraceutical regulations regarding manufacturing, stability, sales, prescription, and assessment of post-adverse events.(10)

The current status of nutraceuticals in Pakistan can be seen as alarming. Inadequate knowledge regarding regulations and unqualified staff for the manufacturing of nutraceuticals are threats to efficacy and quality. The Drug Regulatory Authority of Pakistan has revised the rules for registration, manufacturing, and governing the quality of nutraceutical products named SRO412. Besides, the Ministry of Health directed to prohibit the prescriptions of nutraceuticals over-the-counter to implement the regulations.(11)

In Pakistan, no single study has been reported previously on nutraceutical regulations. This study marks the first exploration report on nutraceutical regulation regarding manufacturing, storage, labelling, and sales practices in major cities of Pakistan. The result of the study reported that the Staff in the manufacturing plant was not qualified for DRAP's requirements. The pharmacist works in every domain of industries, including warehouses, manufacturing units, Quality control labs, and quality assurance. They have expertise in maintaining regulations and standards at every step of manufacturing. In the initial section, no statistically significant (p= 0.496) association was found between the presence of qualified pharmacists in the nutraceutical manufacturing plant. However, DRAP has mentioned hiring pharmacists in the manufacturing unit. The market coverage of most of the industries was limited to local areas. Apart from the availability of pharmacists, most respondents in the current study demonstrated a good understanding of basic nutraceutical concepts p=0.005), and regulations given by DRAP particularly SRO 412, aimed to regulate the sales and import of alternative medicines. DRAP has issued different forms for the enlistment of nutraceutical products. This research indicated that most participants were well-informed about the forms required for application, registration, and provisional certification (p=0.001). However, the study affirmed the respondents' (from Islamabad) lack of specific information about current regulations for alternative medicines. Similar studies were seen regarding the perception of nutraceutical regulations.(12)

Stability is important to maintain the shelf life whether it is a pharmaceutical or nutraceutical product. Common applications are establishing product expiration dates, and ensuring compliance with regulatory standards during stability testing. The product should be compatible with all aspects. Similar guidelines for nutraceuticals can be seen in the recent studies. (13) So, regarding product stability assessments, around two-thirds of participants provided satisfactory responses for reference standards, and therapeutic claims, while one-third of respondents exhibited insufficient knowledge. Most respondents were knowledgeable about nutraceutical labelling requirements, especially concerning contraindications and primary packaging materials.

DRAP has provided some essential guidance to potential manufacturers and importers of therapeutic goods regarding DRAP procedures for enlistment of products. When DRAP's facilitation towards nutraceutical industries was evaluated, the majority of respondents agreed that it is challenging to get listed on Form 6 by DRAP because of strict policies. A study was conducted in the USA on regulatory policies regarding nutraceuticals regulation to prevent unsafe supplements.(14) Responses varied when assessing DRAP's attitude and supportive behaviour especially towards nutraceutical manufacturers. When respondents were questioned about the source of Active Pharmaceutical Ingredients (API), the majority agreed that it must comply with Good Manufacturing Practice (GMP) standards, although opinions diverged on adherence to GMP compliance due to the reluctant behaviour of the manufacturers.

Pharmacists play an important role in the prescription, and dispensing of medicines and provide relevant information

regarding drug use. Their main objective is that consumers receive the correct dose of medicine. The subsequent section revealed that the absence of pharmacists at medical stores can cause problems. data collection was difficult, particularly from medical stores due to owners' reluctance to provide information. The study demonstrates that the participants from (medical stores and pharmacies) were largely unfamiliar with the term “alternative medicine”, often associating it with Spurious or Adulterated products. The unavailability of Pharmacists and inadequate knowledge of workers at medical stores is another barrier to the safe and efficacious use of nutraceuticals. A study was reported in Australia to highlight similar challenges.(15)

Most of the nutritional supplements like food supplements and vitamins were sold under the surveillance of a pharmacist whereas, herbal, Unani, and Ayurveda products were highest in sales where pharmacists were absent. The practice of requiring prescriptions was predominant in locations lacking pharmacists. Only pharmacists were well acquainted with the labelling rules of DRAP Overuse of herbal medicine can affect the quality of life. A detailed report about the safety issues of herbal medicine can be seen in the article.(16) this study revealed that drug inspectors rarely collect nutraceutical samples. According to the International Organization for Standardization, the sample must be collected from the medical stores during the mentioned period to analyse and maintain the stability of Pharmaceutical products. The same regulations should be implemented for nutraceuticals. In Pakistan, certain regulatory frameworks for alternative medicines and, nutraceuticals exist. However, an improvement in the implementation of these regulations is desirable and certainly necessary, and all need to be brought into the mainstream through proper channels. Therefore, there is an urgent need to study further about these regulations.

5. Conclusion

The Study highlights the evolving landscape of nutraceutical regulations in Pakistan and the challenges faced in ensuring the efficacy, quality, and safety of these products. The study emphasizes the critical need for harmonization globally in regulatory frameworks for nutraceuticals, especially concerning manufacturing, storage, labelling, and sales practices. The findings underscore the alarming gaps in knowledge and qualifications among staff involved in nutraceutical manufacturing in Pakistan. While regulatory bodies like the Drug Regulatory Authority of Pakistan have taken steps to enhance oversight through regulations like SRO412, enforcement and compliance remain key issues. Moreover, the study reveals varying levels of understanding and compliance with nutraceutical regulations among industry stakeholders, with notable concerns around stability testing, and labelling requirements of Active Pharmaceutical Ingredients (API).

Pharmacists emerge as crucial stakeholders in ensuring the safe use of nutraceuticals, yet their absence in certain settings poses significant challenges to consumer safety and regulatory adherence. The study also sheds light on misconceptions and practices for alternative medicines in the absence of proper regulatory oversight. Moving forward, there is a clear call for improved implementation and enforcement of existing regulations, and enhancement in collaboration between regulatory bodies, industry stakeholders, and healthcare professionals. Further research and initiatives are essential to address the identified gaps and strengthen the regulatory framework governing nutraceutical products in Pakistan.

6. Limitations

The study on nutraceutical regulations in Pakistan is quite informative, but some limitations should be acknowledged. The insights mainly drawn in major cities may not fully represent the diverse practices and challenges across the entire country. The data collection was limited due to the small sample size and short time, and may not reflect the broader perspective of stakeholders from all over Pakistan. limited depth of information obtained because of the reluctant behaviour of stakeholders. Moreover, the study doesn’t provide longitudinal data on the evolution of nutraceutical regulations in Pakistan over time. A further research, broader stakeholder engagement, and a more comprehensive analysis of nutraceutical regulations could enhance the understanding of the regulatory landscape and contribute to improving the safety and quality of nutraceutical products in Pakistan and beyond.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author Contribution

Farheen Qamer spearheaded the compilation and formatting of the articles and contributed to writing the results and discussions. Tabinda focused on the methodology, while Syeda Muzammil K crafted the introduction. Dr. Muhammad Nabeel reviewed the final manuscript.

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