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Processed Lentil Seed Powder as a Potential Matrix Base for Nutraceutical Tablets

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ABSTRACT

Background and aims: Red lentil seeds (Lens culinaris Medik.) are nutrient rich classified under GRAS, never been used as a matrix base in nutraceutical tablets. This study aimed to characterize processed lentil seed powder (PLSP) as a natural, edible alternative to conventional tablet diluents, with the added benefit of partial nutritional value in the formulation.

Materials and Methods: Red lentil seeds were processed using a high-speed grinder and sieved through a #60 mesh. PLSP was characterized for micromeritics, surface morphology (SEM), crystallinity (XRD), functional groups (FTIR), thermal properties (DSC), microbial load, cytotoxicity (MTT assay), and accelerated stability per ICH guidelines. Placebo nutraceutical tablets were formulated and evaluated for tableting characteristics.

Results: PLSP exhibited good compressibility and flow properties. SEM revealed irregular, porous particles; XRD indicated a semi-crystalline to amorphous structure; FTIR confirmed protein-related functional groups. DSC showed an endothermic peak at 110.36°C. Microbial load was within acceptable limits, and MTT assays showed no cytotoxicity at tested concentrations. Accelerated stability studies revealed PLSP to be fairly stable.

Discussion: The results suggest that PLSP is a promising natural diluent and matrix base for nutraceutical tablets.

Conclusions: PLSP is a safe, functional, and nutritious matrix base for nutraceutical tablets, offering an alternative to synthetic diluents.

Keywords: *Edible alternative, micromeritics, functional groups, safe*

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1. INTRODUCTION

Overview of Nutraceutical Tablet Formulations;

Nutraceuticals, a term introduced by Dr. Stephen L. DeFelice in 1989, refer to food or food parts offering medical benefits, including disease prevention and treatment [1]. Over time, nutraceuticals have grown rapidly in healthcare, bridging the gap between food and pharmaceuticals [2]. Tablets are the most popular dosage form for nutraceuticals like vitamins, minerals, plant extracts, and bioactive compounds, due to better compliance, dose uniformity, stability, and packaging [3].

Formulation Considerations

The development of nutraceutical tablets requires careful selection of excipients (e.g., diluents, binders, disintegrants, and lubricants). Diluents like lactose, microcrystalline cellulose (MCC), and dicalcium phosphate (DCP) are commonly used, but literature has reported adverse reactions such as allergic reactions and gastric irritation, bloating with all of them listed above [4]. Thus, there is a need for natural, safe, and biocompatible diluents that provide acceptable functionality [5, 6].

Scope and Objective of the Study

A literature review revealed the knowledge gap where lentil seed powder has never been used as a tablet diluent for nutraceuticals. This study aimed to explore the potential of processed lentil seed powder (PLSP) as a matrix base for nutraceutical tablets, serving both as a functional excipient and a nutritional ingredient. The objectives are:

1. To process and characterize lentil seed powder (PLSP) in terms of micromeritics [7].
2. To perform various instrumental analyses for in-depth characterization of PLSP [8].
3. To conduct microbial tests to assess the microbial load of PLSP [9].
4. To carry out in vitro toxicity tests on PLSP using selected mammalian cell lines [10].
5. To perform accelerated stability tests on PLSP as per ICH guidelines [11].
6. To compress tablets using PLSP as the matrix base [12].
7. To evaluate the compressed tablets for quality [13].

This study aims to establish PLSP as a natural, safe, and functional alternative to synthetic tablet excipients, contributing to the development of safer nutraceutical formulations [14].

2. MATERIAL AND METHOD

Collection and Processing of Lentil Seed Powder (PLSP*)*

Red lentil seeds were sourced from local markets, cleaned using a compressed air blower, and dried in air. The seeds were then ground into powder using a laboratory grinder and sieved through a #60 sieve. The undersized powder was stored in airtight glass containers inside lab desiccators to prevent moisture absorption [15].

Characterization Methodology

PLSP was characterized through various studies: Micromeritic studies assessed fundamental and derived powder properties [16]. SEM (Scanning Electron Microscopy) examined surface morphology and texture [17]. XRD (X-ray Diffraction) determined the crystallinity [18]. DSC (Differential Scanning Calorimetry) analyzed thermal behavior [19]. FTIR (Fourier-Transform Infrared Spectroscopy) identified functional groups [20]. DLS (Dynamic Light Scattering) measured particle size distribution and zeta potential [21]. Microbial studies assessed total aerobic count and fungal growth as per pharmacopoeial guidelines [22]. Accelerated stability testing followed ICH guidelines [23].

In Vitro Cytotoxicity

The cytotoxicity of PLSP was evaluated on the HaCaT cell line using the MTT Assay [24]. Cells were cultured in 96-well plates for 24 hours and treated with varying concentrations of PLSP, prepared in DMSO and diluted in incomplete cell culture medium. After 24 hours, MTT solution was added, and the cells were incubated for 2 hours. The absorbance at 540 nm was measured using an Elisa plate reader [25]. The IC50 value was calculated using Graph Pad Prism-6. Images were captured under an inverted microscope [26].

Tablet Formulation and Evaluation

Trial batches of uncoated tablets were prepared using PLSP as a diluent along with standard excipients. Three batches were made via direct compression, and three via wet granulation. The tablets were compressed using an 8-station rotary tablet press. The placebo batches were evaluated for tableting properties, and SEM analysis was performed on the tablet core [27].

3. RESULTS

Table 1 : Characterization of processed PLSP

Characterization	Observations, Findings	Remarks
Particle Morphology	Irregular with some fragmented/angular edges. Plate-like morphology.	**Revealed by SEM (Hitachi S4800, 5000X)**
Surface Texture	Rough, coarse, uneven Rough fibrous surface semi-collapsed cell structures	
Shape	Mostly Asymmetric particles	
Fractures & Cracks	Broken crystal-like edges, possibly due to milling or grinding. Micro voids or crevices are visible	
Agglomeration	some particles are loosely clustered	
Color	Light Orange to Peach	
Odor	None	
Moisture Content (%)	2.0- 2.5	Acceptable, Determined by Digital Moisture Balance, AND MX-50

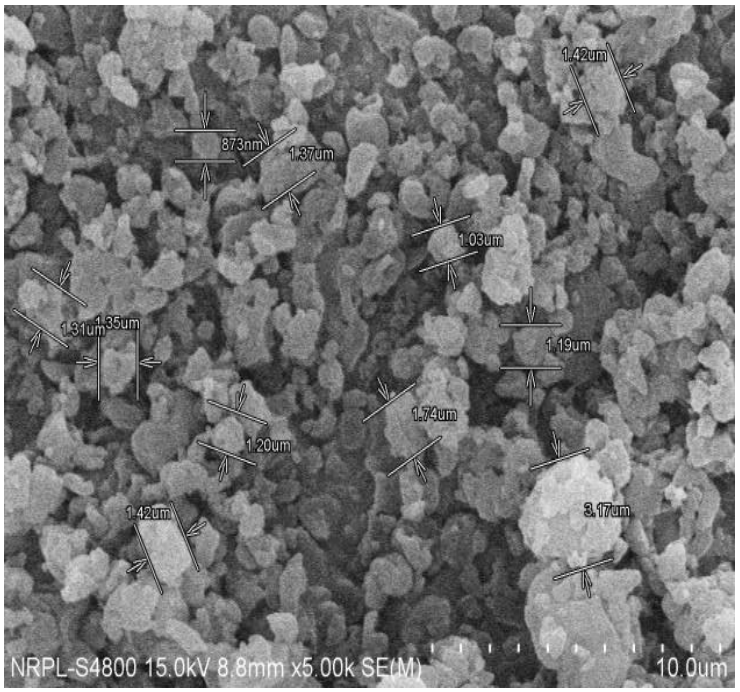


Fig.1: SEM image of Processed LSP revealed Rough fibrous surface semi-collapsed cell Structures (Hitachi S4800, 5000X)

Table 2. Fundamental and Derived Properties of PLSP

Micromeritics	**Observations, Findings**	**Remarks**
Size Range (Particle length)	1.03 to 3.17 micro meter Avg.: 1.52 micro meter	Revealed by SEM (Hitachi S4800, 5000X)
Bulk Density	0.6186 +/- 0.011 g / cm3	Porous, void spaces
Tapped Density	0.8359 +/- 0.005 g / cm3	Moderate packing density
Angle of Repose	39.60 +/- 0.321 °	Fair flow, Determined by classical funnel method
Carr's Index (Compressibility Index %)	25.99 + / - 0.764	Acceptable flow
Haussner's Ratio	1.35 +/ - 0.006	Passable, flow to be improved by addition of optimal amount of glidants, lubricants
Particle Size Analysis on a broader scale	Mean size: 265.2 nm Mode size: 233.4 nm Standard deviation: 78.4 nm **Median Size: 251.9 nm** % Cumulative Distribution: 10% of particles are smaller than 137.7 nm 50% of particles are smaller than 251.9 nm 90% of particles are smaller than 379.0 nm	Mean and mode are relatively close, confirming a consistent size range. **Standard deviation** suggests moderate distribution breadth—not extremely poly-disperse

Polydispersity Index	**PDI: 0.482**	Moderate to high poly-disperse. PDI indicates some heterogeneity in size, possibly due to natural variation in plant-derived compounds or partial aggregation. determined by HORIBA Scientific, sz-100

Instrumental Analysis

Various instrumental analysis viz., XRD, FTIR, DLS and DSC performed on PLSP for further in depth characterization with observations and findings are summarized in **Table 3**. The findings documented in-depth characterization for consideration PLSP as a matrix base for nutraceutical tablets.

Table 3 : Instrumental Analysis on PLSP

Tests	Observations, Findings	Remarks
XRD	d-spacing : ℴ A 20.34501,16.54709,9.26831,5.87697,5.14598, 4.04805,3.76910,3.50478,3.11533,2.95515, 2.87816,2.66173 Anode Material : Copper (Cu) Intended Wavelength Type : K-Alpha	Semi crystalline, Crystalline to Amorphous, determinations revealed patterns which might suggests Nano crystals with hexagonal and orthorhombic crystal structure . Determined by BRUKER D8
FTIR	**Various notable peaks : As depicted in Fig.2** 1600-1700 cm-1, 1500-1600cm-1 1000-1200 cm-1, 1400-1600cm-1 2900–3000 cm-1, 3200-3600cm-1 1100–1150 cm-1, 1100–900 cm^{-1}	Notable Peaks and Valley's corresponds to: Proteins : Amide I, Amide II, Carbohydrates(C-O) C–H stretching Stretching, Phenolic (O-H) (C–O, C–C, and C–O–H stretching) (C–O–H bending) Stretching Determined by SHIMADZU FTIR IRSPIRIT-X Series
DLS	Zeta potential : -27.2 mV Z- Avg. (d. nm) : 2988 nm	Post Dispersion: Moderately Stable Determined by Zetasizer Malvern Instruments Ltd. Indicates the average hydrodynamic diameter of dispersed particles.
DSC	Temperature Range (°C) ***Peak 1*** 83.42 – 110.36 °C	Major endothermic event → moisture loss, protein denaturation, and starch gelatinization. This is a major thermal event, characteristic of: • Initial physical changes (moisture removal), • Structural rearrangement of biomolecules (e.g., protein unfolding), • Beginning of thermally induced biochemical transitions. Minor event → thermal degradation of organic substances. Decomposition of residual organic matter, such as: • Non-protein nitrogenous compounds, • Remaining lipids or phospholipids,

	Peak 2 196.59 – 242.94 °C	• Low-molecular-weight polysaccharides. Revealed by Mettler Toledo 822e

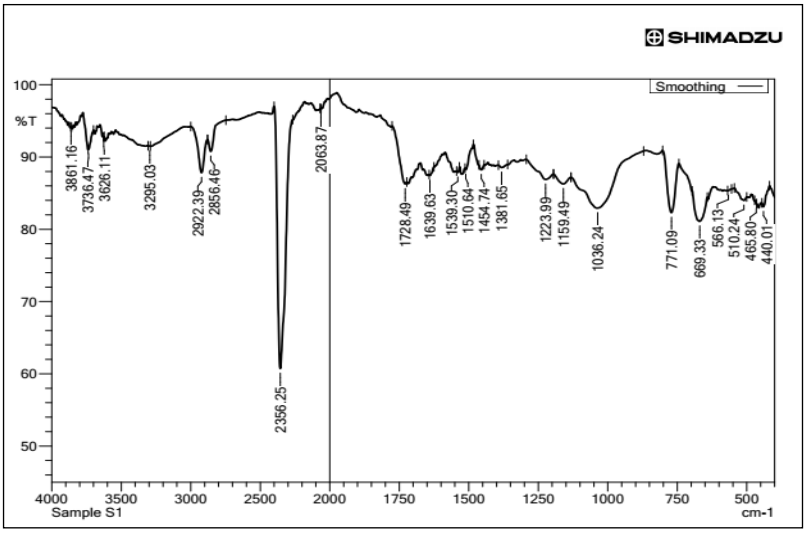


Fig.2. FTIR Spectrum of processed LSP determined by SHIMADZU FTIR IRSPIRIT-X Series

Microbial Studies

Microbial studies revealed that both bacterial and fungal counts were found to be well within the permissible limit ≤1000 cfu/g, as specified by the United States Pharmacopeia, confirming microbiological safety. Total Viable Plate Count in terms of aerobic microbial count was found to be 70 cfu/g, and total combined yeasts/molds count was less than 10cfu/g. *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella spp.* were absent in the sample. Thus, PLSP was found to be safe in terms of microbial contamination [28].

Accelerated Stability studies

The observations and findings are summarized in Table 4. PLSP during the entire study period was found to be stable in terms of physical and micromeritics, with no detectable modification or loss of functional groups in FTIR study. Microbial count remained well within the permissible limit ≤1000 cfu/g, as specified by the United States Pharmacopeia, confirming microbiological safety [29].

Table 4. Record sheet for Accelerated Stability Testing of PLSP as per ICH Guidelines , Q1A(R2),, specifically under accelerated conditions: 40°C ± 2°C / 75% RH ± 5% RH for 6 months

Parameters	Initial, 0 Day	30 Days	60 Days	90 Days	120 Days	150 Days	180 Days
Appearance	Orange Red	No Change	No Change	No Change	No Change	No Change	No Change
Odor	None	None	None	None	None	None	None
Moisture Content (%)	2.0-2.5	2.2-2.5	2.2-2.7	2.2-2.5	2.3-2.5	2.4-2.7	2.5-3.2
BD (g/ml)	0.6186	0.6170	0.6286	0.6089	0.6180	0.5950	0..5988
TD (g/ml)	0.8359	0.8259	0.8153	0.8149	0.8030	0.7947	0.7957
CI (%)	26.00	25.27	22.9%	25.3%	23.0%	25.1%	24.7%
HR	1.351	1.34	1.30	1.34	1.30	1.34	1.33
AOR(θ)	39.6	39.2	38.9	38.63	39.0	38.78	38.52
Microbial Load (cfu/g)	None	Few Colonies	70	89	97	99	103

In Vitro Toxicity

MTT assay was performed using the Human Adult Low Calcium High Temperature (HaCaT) keratinocyte cell line on PLSP [30]. The observations and interpretations revealed that PLSP exhibited no significant cytotoxicity as IC_{50} was not reached within the tested dose range, suggesting excellent biocompatibility and no detectable toxicity, even at the highest tested concentrations [31]. The data indicated it can be considered safe for use as a tablet diluent. The cell viability concentration is represented graphically in Fig.3, and cell viability images at various concentrations of PLSP in DMSO are summarized in Fig.4 [32].

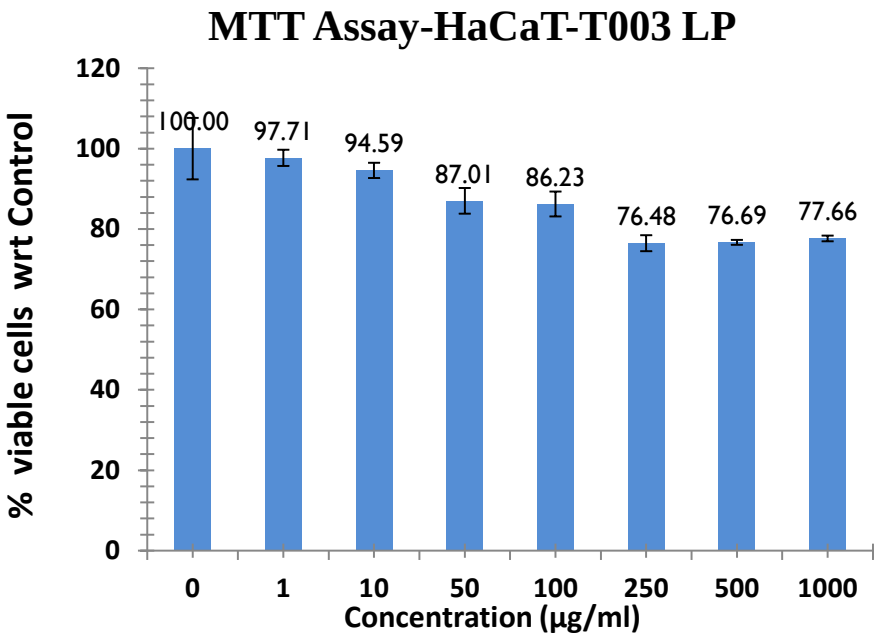
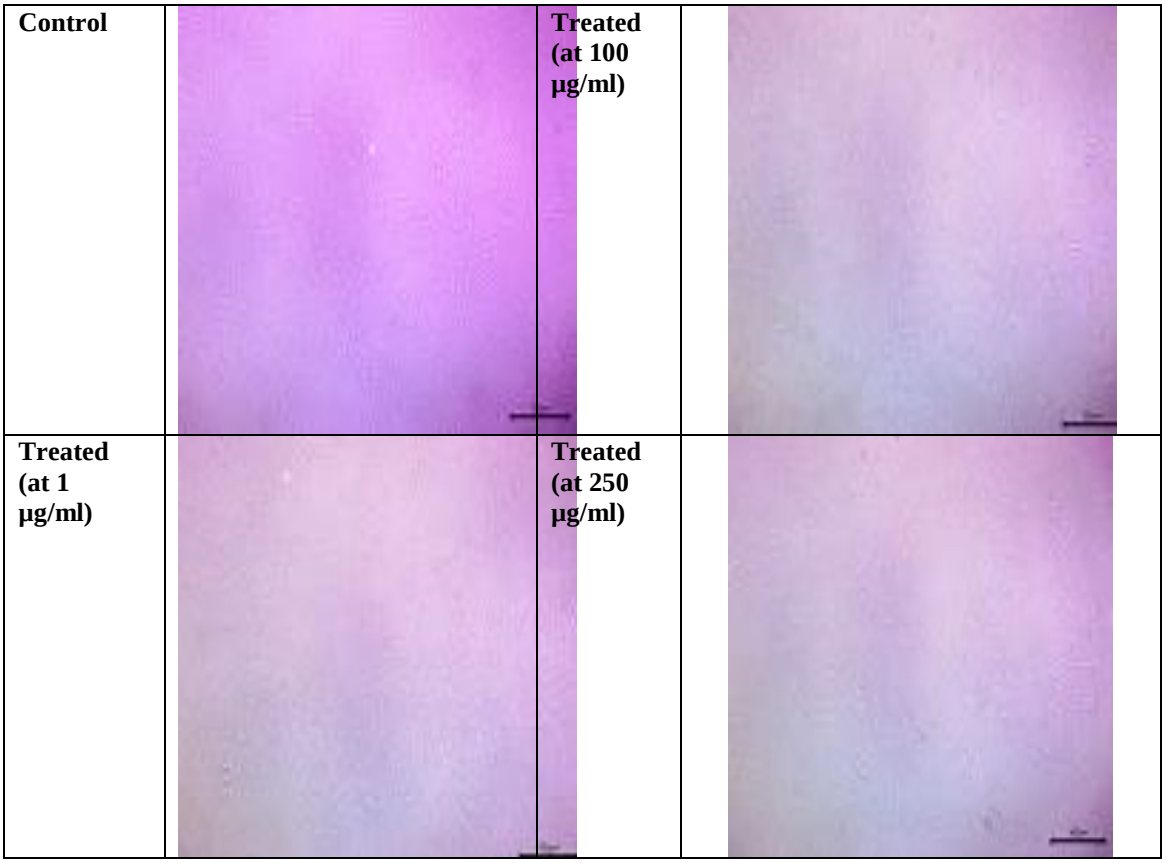


Fig.3. Concentration of PLSP in DMSO vs. % Viable cells with respect to control



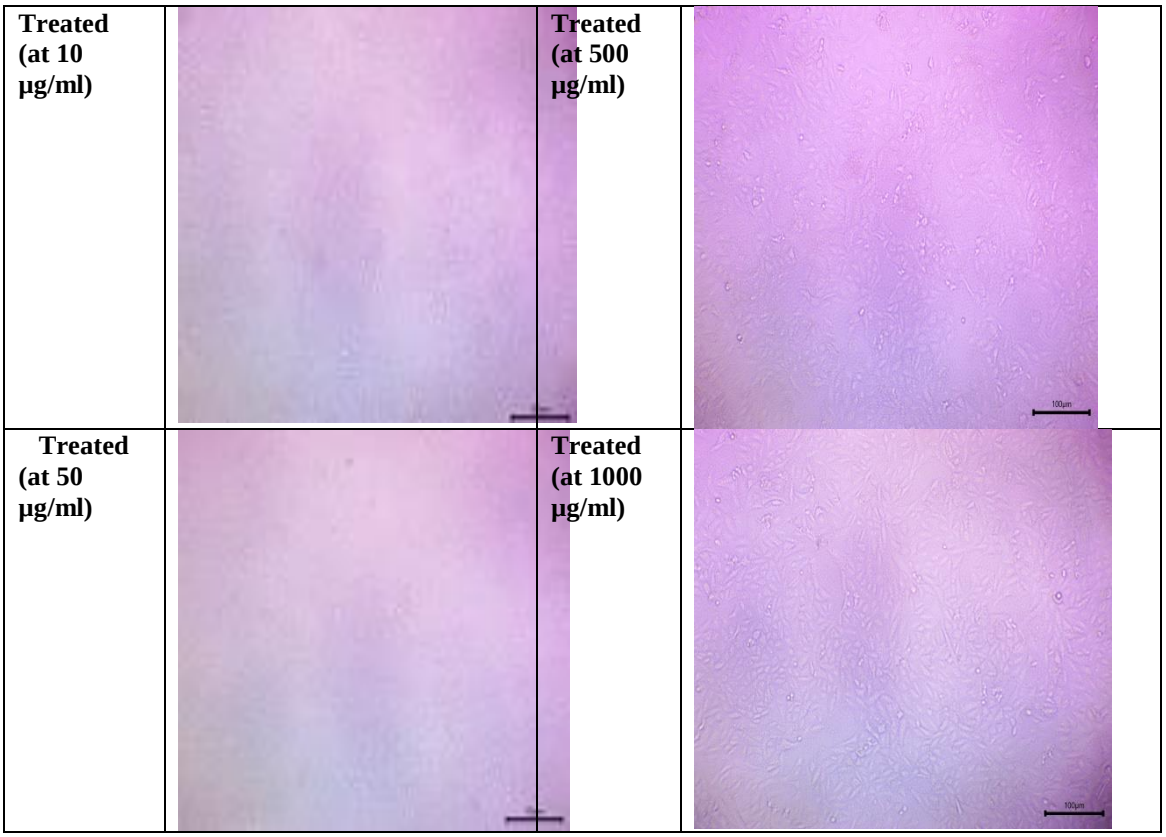


Fig. 4. MTT Assay Microscopy using HaCaT Cell line, % Viable Cells Vs. Concentration of PLSP, Cell Viability Images (MAGNIFICATION 100X)

Formulation and Evaluation of Compressed Tablets

Six placebo trial batches of tablets were prepared. Three batches were prepared by direct compression (F1–F3) and three by wet granulation (F4–F6), while direct compression involved sieving, bolting of lubricant mix, blending, and compression. Wet granulation employed a non-aqueous granulation technique, whereby binder, PVP K-30, was activated with Isopropyl Alcohol, and granulation was carried out [33]. Dried granules were sieved through #30 screen and blended with bolted lubricant mix and compressed. An 8-station rotary tablet press was used for the compression. Formulations are summarized in Table 5. Tableting was achieved for all the formulae with no apparent tableting defects observed during compression with acceptable flow of blends. Evaluation of all the placebo batches is summarized in Table 6 [34]. All the batches demonstrated acceptable tableting properties with PLSP showing optimum functionality in terms of matrix base. Statistical analysis performed on the data obtained for tableting properties is summarized in terms of hardness [35]. ANOVA depicted a significant difference ($p < 0.05$) among formulations. F6 had the highest hardness (5.54 kg/cm²), while F3 showed the lowest (3.87 kg/cm²). Batches F5 and F6 were significantly harder compared to F1–F3, indicating stronger compaction in wet granulation. In terms of friability, no significant difference was observed

($p > 0.05$); all batches remained below 1%, well within Pharmacopeial limits, confirming good mechanical resistance. Disintegration time analysis revealed highly significant differences ($p < 0.01$). Placebo batches (F1–F3) disintegrated fastest (<0.5 min), while drug-loaded batch F7 and wet granulated batch F6 showed prolonged disintegration (>1.3 min). Interpretation of data revealed significant differences in hardness and disintegration time ($p < 0.05$). The data analysis and interpretation are summarized in Table 7 [36]. F1 (direct compression) showed the lowest disintegration time with acceptable hardness and friability, while F5 (wet granulation) demonstrated the lowest friability and optimal hardness. Tableting properties were found to be satisfactory for all the batches. SEM of tablet cores revealed a porous internal structure (Fig.5), indicating a matrix bed presence [37].

Table 5. Formulation of Placebo Trial Batches of Tablets

Ingredients	***F1***	***F2***	***F3***	***F4***	***F5***	***F6***
	Quantity in mg					
PLSP	250	300	350	250	300	350
Hydroxy Propyl Methyl Cellulose E5	30	50	40	---	---	---
Polyvinylpyrrolidone (PVP K-30)	---	---	---	12	14	16

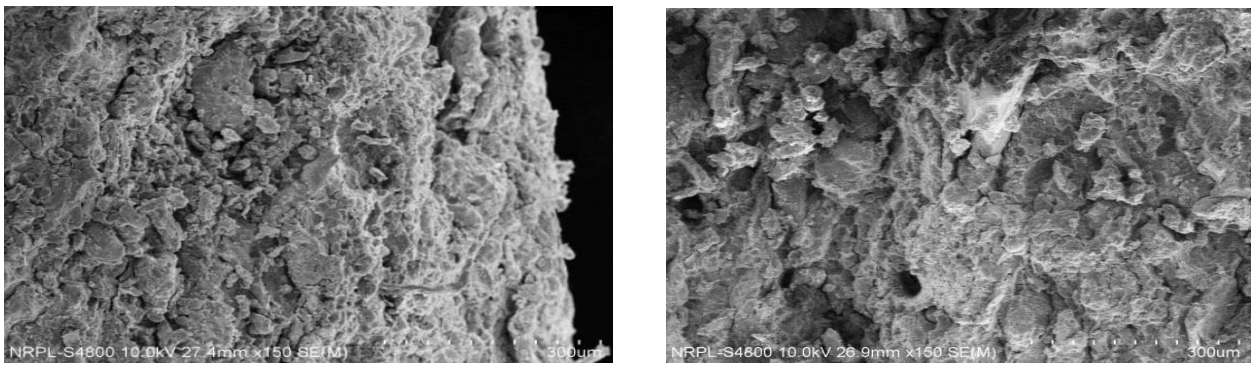
Cross Carmellose Sodium	40	40	40	40	40	40
Iso Propyl Alcohol	---	---	---	***qs***	***qs***	***qs***
Talc	10	10	10	10	10	10
Magnesium Stearate	10	10	10	10	10	10
Aerosil	1.0	1.0	1.0	1.0	1.0	1.0
AVG WT PER TABLET (mg)	341	411	451	323	375	427

Table 6. Evaluation of Placebo Tablets Prepared with PLSP as Matrix base

Parameters	**F1**	**F2**	**F3**	**F5**	**F6**	**F7**
Shape	Bi-concave	Bi-concave	Bi-concave	Bi-concave	Bi-concave	Bi-concave
Thickness (mm)	3.91 – 3.95	4.11 – 4.24	4.68 – 4.71	3.20-3.31	3.52-3.58	3.78-3.83
Diameter (mm)	11.0	11.0	11.0	11.0	11.0	11.0
Hardness (Kg/cm3) Mean	4.0 – 4.4 4.23±0.208	4.6- 4.8 4.70±0.100	3.8- 4.2 3.87±0.306	5.1 – 5.3 5.233±0.115	5.5 – 5.6 5.54±0.058	4.8- 5.1 4.934±0.153
Friability (%) Mean	0.49-0.62 0.564±0.067	0.46-0.49 0.476±0.015	0.62-0.71 0.657±0.047	0.40-0.45 0.427±0.025	0.43-0.47 0.446±0.021	0.52-0.55 0.537±0.015
Weight Variation (±5 %)	Within Limits	Within Limits	Within Limits	Within Limits	Within Limits	Within Limits
Disintegration Time (min)	0.45 – 0.48 0.466±.015	0.43 – 0.46 0.456±0.015	0.47 – 0.49 0.483±0.012	1.58-1.59 1.583±0.006	1.37-1.38 1.373±0.006	1.60-1.66 1.630±0.030

Table 7. Statistical Basis (One-way ANOVA) of Comparison of Tableting Properties

Parameter	**F-value**	**P-value**	**Interpretation**
Hardness	511.63	1.51×10^{-13}	Highly significant difference between batches ($p < 0.001$)
Friability	9.42	7.73×10^{-4}	Significant difference between batches ($p < 0.001$)
Disintegration	286.43	4.77×10^{-12}	Highly significant difference between batches ($p < 0.001$)



A B

Fig 5. ***SEM images of PLSP tabs, (Hitachi S4800, 5000X),***
A. F1 , Placebo tablets prepared by direct compression
B. F5 , ***Placebo tablets prepared by wet granulation***

4. DISCUSSION

Material Characterization and Surface Morphology

SEM analysis showed that PLSP has an irregular, plate-like morphology with rough, fibrous texture and semi-collapsed cell structures, likely due to mechanical processing. These features enhance compressibility and interlocking during compaction [38]. The low moisture content (2.0–2.5%) contributes to improved shelf stability, while the light orange to peach coloration increases consumer acceptability in nutraceutical applications [39].

Micromeritic and Flow Properties

PLSP displayed acceptable bulk and tapped densities, moderate angle of repose, and compressibility index, indicating good flow and compaction behavior [40]. This suggests PLSP could serve as a natural, cost-effective alternative to conventional excipients like MCC, which shows similar flowability [41].

Instrumental Analysis and Structural Characteristics

XRD revealed semi-crystalline characteristics, suggesting both ordered and amorphous regions, which contribute to the excipient's functional versatility [42]. FTIR analysis identified proteins, carbohydrates, phenolics, and polysaccharides, supporting PLSP's potential bioactivity and binding capabilities for nutraceutical applications [43]. DLS showed a Z

Microbial Safety

Microbial analysis showed excellent safety, with total aerobic count (70 cfu/g) and yeast/mold count (<10 cfu/g) well within USP limits. The absence of pathogenic bacteria like E. coli, S. aureus, and Salmonella confirmed PLSP's suitability for oral formulations.

Accelerated Stability Studies

The stability study revealed that PLSP maintained its appearance, moisture content, and flowability over six months. While the moisture content slightly increased (2.0-3.2%), it remained within acceptable limits, with only minor fluctuations in bulk and tapped densities [44]. The compressibility index remained stable, indicating consistent powder behavior [45]. The microbial load increased slightly to 103 cfu/g by day 180, which warrants monitoring, but remains within acceptable limits [46]. Overall, PLSP showed good stability, making it a promising excipient for nutraceutical tablets [47].

In vitro Cytotoxicity

The MTT assay confirmed that PLSP is non-cytotoxic to HaCaT cells, even at high concentrations [48]. The IC_{50} was not reached, demonstrating high biocompatibility [49]. Similar findings were reported for other plant-based excipients, supporting PLSP's suitability for human use [50].

Tablet Formulation and Performance Evaluation

PLSP was successfully incorporated into both direct compression and wet granulation processes. Wet granulated tablets showed higher hardness (up to 5.54 kg/cm²), while direct compression batches exhibited faster disintegration (<0.5 min), suggesting application-specific benefits. ANOVA revealed significant differences in hardness and disintegration ($p < 0.05$), but friability remained below 1%, indicating good mechanical strength.

SEM of tablet cores showed a porous matrix, which supports disintegration and dissolution behavior due to increased surface area.

Comparative Perspective and Implications

PLSP offers several advantages over conventional excipients like lactose or MCC: it is naturally derived, semi-crystalline, and has inherent bioactivity, which aligns with the growing demand for clean-label, plant-based excipients [51]. PLSP enhances both mechanical properties and bioactivity, making it a valuable option for nutraceutical formulations [52].

Strengths, Limitations, and Future Perspectives

The study's strength lies in its comprehensive characterization of PLSP, using advanced techniques (XRD, FTIR, DLS, DSC, SEM). However, the absence of in vivo data limits its industrial scalability. Future studies should include animal studies to further validate PLSP's performance in live systems.

5. CONCLUSION

In this research, processed red lentil seed powder (*Lens culinaris*) has been investigated as a possible natural diluent for nutraceutical tablets as an alternative natural tablet diluent. As stated earlier , red lentil seeds were processed and finely grounded into powder and characterized in terms of micromeritics, surface morphology (SEM), crystallinity (XRD), functional groups (FTIR), phase changing properties (DSC), microbial load and *In vitro* cytotoxic study (MTT). The

findings PLSP as diluent with other standard tablet additives were used to compress tablets using 8 station rotary tablet press. SEM revealed irregular particles with a porous nature, whereas XRD confirmed semi crystalline, crystalline and amorphous nature. FTIR spectra confirmed the presence of functional groups consistent with pulses in terms of proteins. DSC determination revealed first endothermic reaction over 110.36 °C. Microbial studies demonstrated bacterial, fungal growth was well within limits. *In vitro* toxicity studies revealed PLSP had no noticeable cytotoxicity, even at the highest tested concentrations. Placebo tablets prepared with PLSP as a diluent demonstrated matrix base functionality with no tableting defects observed during compression. Tablets prepared by direct compression and wet granulation depicted PLSP as a satisfactory bulk former or diluent with a optimal mechanical strength. Thus, present research proposes PLSP as a suitable matrix base for nutraceutical tablet formulations.

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Abbreviations used in the text;

GRAS **--Generally Recognized As Safe.**
SEM – Scanning Electron Microscopy
XRD – X-ray Diffraction
FTIR – Fourier Transform Infrared Spectroscopy
DSC – Differential Scanning Calorimetry
MTT – 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT assay for cell viability)
MCC – Microcrystalline Cellulose
DLS – Dynamic Light Scattering
ANOVA – Analysis of Variance
HaCaT – Human Adult low Calcium high Temperature keratinocytes (an immortalized human Keratinocyte cell line)
cfu – colony forming unit