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Phytonutrient formulation using gum Arabic and *Adansonia Digitata* pulp: Lessons for boosting the human immune system - part 1

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ABSTRACT

Background: The human innate immune system (HIIs) defends the body against pathogens and relies on the energy obtained from food sources to increase its metabolic activity.
Aim: In this study, a new blended 3 in1 formula comprising *A. senegal, A. seyal*, and Adansonia digitata at a ratio of 5:3:2 was proposed as a potential aid in the management of Covid-19 patients with Metabolic Syndrome (MeT-S) disorders, with a specific focus on those presenting with impaired health.
Methods: The utilization of Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-MS) was employed to analyze 3 blended ingredient combinations, including the 3in1 formula, *A. senegal, A. seyal*, and *A. digitata* pulp, for the presence of elements by detecting the levels of moisture, ash, minerals, protein, amino acids, carbohydrates, sugars, prebiotic polysaccharides, energy, dietary fibers, and crude fibers. This advanced technique has replaced the titration method used in previous studies.
Results: The mineral content of the blended 3in1 sample was found to be dominated by potassium (70.56±2.35), Calcium (68.54±3.12), Magnesium (16.60±4.80), Phosphorus (11.50±2.50), Sodium (31.4±4.80), Zinc (19.19 ±2.10), Iron (19 ± 0.14), Copper (15.12±1.81), and selenium (0.037 ± 0.005) g/100 g DW. The blended 3 in1 sample also had a higher hydroxyproline content (30.17 g/100 g and a higher total protein and carbohydrate content than the blended 2 in1 sample. Additionally, arabinose was identified as the major reducing sugar with up to 48.23 and 49.97g/100 gDW. The prebiotic polysaccharide content was 88.61±3.12g/100 gDW for the blended 3 in1 sample, which was significantly higher than that of the blended 2 in1 sample. Furthermore, the energy value of the blended 3 in1 sample was significantly higher at 350.12±5.210 kcal/100 g than the blended 2 in1 sample at 340.67±3.155 kWh. The Insoluble Dietary Fibers (IDFs) and Soluble Dietary Fibers (SDFs) of the blended 3 in1 sample were 12.6±2.10 g/100 gDW and 87±2.124 g/100 g DW, respectively, which were significantly higher than those of the blended 2 in1 sample.
Conclusion: The discovery of distinct molecular compositions of *A. senegal* and *A. seyal* when combined with *Adansonia Digitata* Pulp (ADLP) in the 3 in1 blend demonstrated enhanced HIIs among Covid-19 patients with compromised MeT-S disorders. This may be considered a valuable natural antiviral agent for the treatment of such individuals.

Abbreviation

ACE	Angiotensin I-converting enzyme
ANOVA	Analysis of Variance
AOAC	Association of Official Analytical Chemists
BERC	Bioenvironmental Engineering Research Center
CCB	Calcium Channel Blocking
DF	Dietary fibers
DW	Dry weight
EAA	Essential Amino Acids
FDA	Food and Drug Administration
FNP	Formulations of Natural Prebiotics
HII	Host immune
IDF	Insoluble dietary fibers

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IsDB	Islamic Development Bank
ND	Not detected
NEAA	Non-Essential Amino Acids
NPF	Natural prebiotic formulations
PF	Pulmonary Fibrosis
PP	Prebiotic polysaccharides
PV	Proximate values
SDF	Soluble dietary fiber
SDG	Sustainable Development Goals
WHO	World Health Organization

1. Introduction

The World Health Organization (WHO) declared Covid-19 a global health crisis on January 30, 2020, and officially characterized it as a pandemic on March 11, 2020. As of August 19, 2024, there were 775,867,547 confirmed active cases of Covid-19 and 7057,145 reported deaths (WHO, 2024). Extensive research has shown that organic medicine does not significantly affect the clinical course of the virus even in 180 countries (Huang *et al.*, 2020a). Therefore, there is a need to explore other beneficial approaches such as the use of prebiotic-rich foods. A severe condition is called the Metabolic Syndrome (MeT-S) of the immune system (Fahed *et al.*, 2022). MeT-S refers to a group of health problems with long-lasting effects (Hachiya et al., 2022). These include high blood sugar levels, high blood pressure, excessive body fat, and abnormal cholesterol and triglyceride levels (Fahed et al., 2022). Individuals with Covid-19 and MeT-S require extra medical attention because they have a higher chance of developing heart disease, stroke, and uncontrolled diabetes (Alotaibi *et al.*, 2023). Consequently, integrating dietary management strategies that target MeT-S could be essential in mitigating the exacerbated health risks associated with Covid-19 in affected populations.

According to several studies, the human gut contains more bacteria than the other cells in the body. This insight has illuminated the relationship between selenium levels in this area and documented cases of Covid-19 in China (Fakhrolmobasheri *et al.*, 2022; Sender *et al.*, 2016; Wang *et al.*, 2023c). The gut health of individuals infected with Covid-19 can improve by preventing the spread of harmful bacteria (Petakh et al., 2023). This can help the immune system reduce symptoms (Xu *et al.*, 2020; Yeoh *et al.*, 2021). Preventing a decline in intestinal mucosal health can improve bowel function and reduce diarrhea (Tamvakeras *et al.*, 2023). Research has found that the immune system of Covid-19 patients can be strengthened, and their reliance on antibiotics is reduced by probiotics (Yang *et al.*, 2020a; Zyoud *et al.*, 2023). Acacia gums (AG) may lower the risk of spreading intestinal bacteria and infections from the mouth to other body parts (Momo Cabrera *et al.*, 2024). Therefore, increasing selenium levels and using probiotics and prebiotics, such as AG, could strengthen immunity and gut health in Covid-19 patients.

Food has multiple biological benefits such as improving the host immune system (HIIs). Specific dietary supplements such as prebiotics and vitamin D have been suggested to amplify the therapeutic effects of Covid-19 (Alipio, 2020; Hosseini *et al.*, 2022; Vishwakarma *et al.*, 2022). Although supplements can provide protection against Covid-19 (Burki, 2022), no single food can prevent viral infections entirely (Bhatta, 2020). Food and pharmaceutical industries are increasingly interested in natural prebiotic formulations (NPFs). One study found that consuming NPFs from *Acacia senegal* and *Acacia seyal* as part of a healthy diet could increase HIIs, especially in individuals with weakened immune systems (Ahmed *et al.*, 2023; Kaddam and Kaddam, 2020). Polyphenols in NPFs regulate the production of cytokines including TNF-α and IFN-γ by activating adenosine A2A receptors (Bottari *et al.*, 2019; Efferth *et al.*, 2022). Therefore, the addition of NPFs to the diet can improve health and reduce the risk of various illnesses.

Many biological studies have focused on *A. senegal* and *A. seyal* owing to their essential roles. Thorough research has shown that *A. senegal* and *A. seyal* play an ongoing role in enhancing lipid metabolism, a discovery that dates back to 1992. This feature may prevent kidney failure and other degenerative diseases (Al Za'abi *et al.*, 2018), especially in metabolic or cardiovascular conditions (Jarrar *et al.*, 2021). These plants help to fight inflammation (Elnour *et al.*, 2018) and cancer (Elnour *et al.*, 2019). They are not only used to study gastrointestinal disorders (Wapnir *et al.*, 2008). These plants also contain antioxidants (Elnour *et al.*, 2022). *A. senegal* and *A. seyal* have antiviral properties that can be used to treat tapcovirus (Joly, 1952) and *Plasmodium* malaria virus (Ballal *et al.*, 2011). Thus, *A. senegal* and *A. seyal* are critical for developing treatments for a range of conditions, from metabolic disorders to infectious diseases, owing to their diverse therapeutic properties.

Promising evidence suggests that *A. senegal* and *A. seyal* are potent immunoregulatory agents for individuals with Covid-19 that provide significant benefits (Pratedrat *et al.*, 2023). These plants can address latent viruses stored within cell reservoirs, such as brain and lymphoid tissues, demonstrating their therapeutic potential (Kaddam and Kaddam, 2020). *A. senegal* and *A. seyal* within the body elevates the concentration of advantageous *Bifidus* and lactic acid bacteria. As a result, various research teams have explored their use in managing Covid-19, and 20% of patients with gastrointestinal symptoms such as diarrhea and abdominal pain are typically linked to viral infections (Dong-ling *et al.*, 2022). Therefore, it is important to reconsider food formulations to strengthen the immune response. The exceptional prebiotic nature of ADLP, along with its diverse biological functions and antioxidant properties, are noteworthy. Historically used in food and medicine, baobab provides vital nutrients such as vitamins A and C (Abuljadayel, 2023). ADLP serves as a valuable reservoir of calcium, potassium, and dietary fiber (Ahmed *et al.*, 2024). Previous research has shown its effectiveness in addressing gastrointestinal disorders (Lehmann *et al.*, 2021) and alleviating symptoms associated with Metabolic Syndrome (Salih *et al.*, 2024). Thus, using *A. senegal* and *A. seyal* in diets could boost immunity and gut health in Covid-19 patients, capitalizing on their prebiotic and antioxidant benefits.

The Covid-19 pandemic has emphasized the importance of a strong immune system to effectively fight infectious diseases (Manna *et al.*, 2022). Malnutrition-induced infections can severely compromise immune function, especially in vulnerable populations (Zemrani *et al.*, 2021). To enhance immune responses against Covid-19, prior research has devised NPFs using valuable resources, such as *A. senegal, A. seyal*, and ADLP. Blended compositions encompass immunization and detoxification mechanisms, rendering them efficacious treatment options. The diverse range of phytonutrients with varying effects on human health further emphasizes the potential significance of polyphenolic content in Formulations of Natural Prebiotics (FNPs) (Khalil and Tazeddinova, 2020). Individuals affected by latent viral infections can benefit from the utilization of organic plant materials, which facilitate the removal of dormant viruses from diverse cellular reservoirs encompassing the brain and lymphoid organs (Kaddam *et al.*, 2020). Therefore, using natural prebiotics, such as *A. senegal, A. seyal*, and ADLP, in diets can strengthen immunity and detoxify the body, which is key for combating latent viral infections and improving health.

Shohag *et al.* revealed that FNPs are antioxidants that combat detrimental free radicals that might harm neurological cells (2022). This discovery could revolutionize health benefits and create over 25,000 plant-based food products, particularly those based on FNPs (da Silveira Vasconcelos *et al.*, 2020). Considering this, the current study proposes the introduction of a novel blend containing *A. senegal* and *A. seyal* (a combination of *A. senegal* gum and *A. seyal* gum), along with ADLP. This study aimed to assess its effectiveness in enhancing host immune responses (HIIs) in asymptomatic Covid-19 patients. The methodology employed in this study follows an ethnopharmacological approach to enhance the Host Immune Index (HII) of individuals with Covid-19 who also have MeT-S. A standardized methodology was used to examine the molecular composition of the essential minerals, functional proteins, complex carbohydrates, prebiotic polysaccharides, effective energy sources, and dietary fibers in the blended formulation.In developing nations, accessible and cost-effective food sources play a pivotal role in providing essential nutrients to vulnerable populations. The results of this study hold promise for the development of evidence-based approaches to improve public health, reduce the consequences of infectious diseases, and promote Sustainable Development Goals (SDGs), notably SDGs3 and 4 (Angela et al., 2023; Grosso et al., 2020). Thus, accessible and affordable food in developing nations is key to better nutrition, disease control, and achieving SDGs 3 and 4.

2. Materials and Methods

2.1. Collection and Preparation of the Optimum Formula

We gathered initial samples containing *A. senegal* and *A. seyal* gums, along with ADLP, from the Blue Nile state in Sudan (coordinates:11°16′N, 34°4′E) during the 2019/2020 season. To ensure a comprehensive comparison, we formulated 3 modified ADLP combinations: optimal blend, specific blend, and baseline blend (3 in1, 2 in1, and 1 in1). The coordinated 3 in1 mixtures comprised *A. seyal, A. senegal* gums, and ADLP powder. In contrast, the blended 2 in1 mixes combined only *A. senegal* gum with Prebio-M derived from *A. seyal* gum. To guarantee the absence of natural impurities, such as bark and sand, we randomly selected each sample and divided them into 3 segments. The segments were ground and powdered using a 1.40 mm metal sieve from Fisher in Lenexa, Kansas, USA. *A. senegal* (5 g), *A. seyal* (3 g), and ADLP (2 g) were used for further analysis.

2.2. Optimum formula nutritional values Determination

2.2.1. Moisture content determination

Accurate moisture content was determined following the Association of Official Analytical Chemists (AOAC) method with slight adjustments, as described by Horwitz and Latimer (2005). The moisture content was assessed in triplicate using STP/Chem/A04, an internal method based on the AOAC's 16th edition, Section 950.46. Initially, the crucibles were dried in an empty Heraeus oven at 105°C for 30 min. After cooling, the crucibles were weighed using a desiccator (M1). Approximately 2 g of the sample was weighed (M2).

Subsequently, the contents were oven-dried at 105°C for 5 h and allowed to cool in a dryer before the final weight (M3) was measured. The percentage of sample loss owing to the drying process was computed using equation [1], as outlined below:

$$\text{Moisture (\%)} = \frac{\text{M3} - \text{M2}}{\text{M1}} \times 100 \quad (1)$$

Where M_1 is the weight of the empty crucible, M_2 is the weight of the crucible and raw sample, and M_3 is the weight of the crucible and the dried sample.

2.2.2. Ash content determination

We followed the AOAC 17th Edition guidelines to determine the ash content and used our in-house STP/Chem/A02 method (AOAC, 2006a). To achieve this, the samples were carefully placed in crucibles that were initially weighed and labeled W1. The crucibles were then heated overnight at 550°C (Carbolite CSF 1200) in an electronic muffle furnace. After this process, the crucibles were cooled to a desiccator before being weighed again and labeled W2. The total ash percentage was calculated using equation [2].

$$\text{Total Ash (\%)} = (\text{W3} - \text{W1}) / (\text{W2} - \text{W1}) \times 100 \quad (2)$$

where W1 is the empty crucible, W_2 is the crucible and sample, and W_3 is the dried crucible and the sample. This method accurately determined the ash content and nutritional composition of samples.

2.2.3. Mineral profile evaluation

Mineral content analysis was conducted by microwave digestion and inductively coupled plasma. This methodology was used to quantify the concentrations of diverse minerals (such as calcium, magnesium, potassium, sodium, zinc, copper, and cadmium) and heavy elements (including arsenic, mercury, cadmium, antimony, lead, tin, zinc, selenium, chromium, manganese, phosphorus, copper, and iron) present in the sample. The process outlined in 1999 followed the procedure established by Miller *et al.*(1998), with slight adjustments. To ensure precision, the analysis was conducted in triplicates. The samples were dried at 105°C for 30 min until reaching a consistent weight. Subsequently, 2 mL of 35% hydrogen peroxide (H_2O_2) and 5 mL of 65% nitric acid (HNO_3) were added to the samples in a sealed microwave system (Cem-MARS Xpress, Australia). The subsequent phase entailed assessing the mineral concentrations using an Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-MS) instrument, specifically the Varian-Vista model in Australia. This was achieved by digesting the sample with ultra-deionized water and adjusting the total volume to 20 mL. To determine the metal concentration based on ICP-MS readings, equation [3] was used:

$$\text{Metal concentration} = (\mu g / L) / W \times V \quad (3)$$

This equation uses symbols to represent the values. μg/L (ppb), W (0.5 g, and V (25 mL).

2.2.4. Protein and amino acids profile Quantification

In-house method No. STP/Chem/A03, based on the AOAC 16th subcomponent 981.10 (Act, 1983; AOAC, 2006b), was employed to determine the protein content. Following the measurement of the sample to the nearest 0.5–2 g, a mixture of 15 mL sulfuric acid (H_2SO_4) was added, and it was subsequently digested and titrated using the Kjeldahl method. In this process, nitrogen is converted into ammonia (NH_3) by treatment with concentrated H_2SO_4 and orthophosphoric acid (H_3PO_4), with copper sulfate ($CuSO_4$) and potassium sulfate (K_2SO_4) serving as the catalysts. Ammonia was vaporized and condensed into boric acid after treatment with NaOH. This was quantified using hydrochloric acid. The ACCQ-TAG method was used to analyze amino acid profiles following the approach of Bougatef *et al.* (2008). Sample preparation included weighing the defatted samples (ranging from 0.1 to 0.2 g) and adding 5 mL of 6 N HCl to a test tube. The samples were then placed in a container and heated in an oven at 110 Â°C for 24 h. After cooling to room temperature, the sample was filtered into a 100 mL flask and mixed with 400 mL of 50 mol AABA (internal standard) and 100 mL of deionized water. Following filtration, [4] was used to extract the sample in a centrifuge tube.

$$\text{Amino acids}\left(\frac{\text{mg}}{100\text{ g}}\right) = \frac{\text{mg of amino acid content in the sample}}{(\text{mg of the same amino acid in reference protein}) \times 100} \quad (4)$$

The method used for assessing the protein content and amino acid profile was an in-house procedure known as No. STP/Chem/A03, which follows the guidelines outlined in the AOAC 16th sub-component 981.10 (Act, 1983; AOAC, 2006b). The sample was weighed (approximately 0.5–2g) and mixed with 15 mL of sulfuric acid (H_2SO_4) for protein content determination. The mixture was then subjected to digestion, distillation, and titration using the Kjeldahl method. Concentrated H_2SO_4, H_3PO_4, $CuSO_4$, and K_2SO_4 helped convert nitrogen in the sample to ammonia (NH_3). The mixture was treated with sodium hydroxide to create boric acid, and the resulting alkalinity caused the steam distillation of ammonia. Hydrochloric acid (HCl) was used to titrate boric acid. The ACCQ-TAG method was used to analyze the amino acid profile following the approach outlined by Bougatef *et al.* (2008). Sample preparation involved weighing defatted samples (approximately 0.1 to 0.2 g) and adding 5 mL of 6 NHCl to a test tube. The model in the test

Table 1
Chemical characterization of the optimal formula consisting of *A. seyal* and *A. senegal* gum (PMC and PTC) powder and ADLP powder.

Nutritional Values	PMC&PTC (Blended 2 in 1) Mean ± S.D	ADLPs	Optimum formula (Blended 3 in 1)
Moisture (%)	11.51±0.150[a]	10.57±1.02[b]	11.0±1.350[c]
Total Ash (%)	3.48±0.0050[c]	04.5±0.3000[a]	4.0±1.2000[b]
Fat (g/100gDW)	0.0133±0.0059[c]	0.30±0.0223[a]	0.30 ±0.0019[a]
Cholesterol (g/100gDW)	N.D.	0.1±0.00120[a]	0.1±0.0015[a]
Prebiotic Polysaccharide (g/100gDW)	84.00±2.15[b]	80±3.20000[c]	88.61±3.1210[a]
Protein (g/100gDW)	2.363±0.0058[c]	2.5±0.11200[b]	3.34±0.12100[a]
Carbohydrate (g/100gDW)	84.34±4.577[b]	78.40±2.000[c]	86.32±3.1120[a]
Energy (k cal/100g)	340.67±3.155[b]	322.5±5.200[c]	350.12 ±5.210 [a]
Soluble DFs (g/100gDW)	84±30.45000[b]	48±1.30000[b]	87±2.123500[a]
Insoluble DFs (g/100gDW)	1.865±0.0050[c]	6.73±1.023[c]	12.62 ±2.100[a]
Crude fiber (g/100gDW)	0.0133±0.0058[c]	12.62±1.300[b]	12.82±1.700[a]
Acid Insoluble Residue (g/100gDW)	0.9100±0.0120[b]	0.90±0.0110[c]	0.95±0.01560[a]

Note: * Mean value ± SD in raw, followed by different superscript letters accurately shows a significant difference ($p \leq 0.05$) between rows. **PMC**, *A. senegal* gum (commercial); **PTC**, *A. seyal* gum (commercial); **ADLP**, *A. digitata* pulp powder; **ND**, not detected.

tube was heated in an oven at 110°C for 24 h. After cooling to room temperature, the sample was transferred to a 100 mL volumetric flask via a filter funnel. The flask was filled with 400 mL of 50 mol AABA (internal standard) and 100 mL deionized water. At the end of the procedure, a small portion of the sample (10μL) was filtered and transferred to a vial for subsequent processing. Equation [4] was used for this process.

$$\text{Amino acids}\left(\frac{\text{mg}}{100\ \text{g}}\right) = \frac{\text{mg of amino acid content in the sample}}{(\text{mg of the same amino acid in reference protein}) \times 100} \tag{4a}$$

$$\text{Energy (kCal / g)} = (4\ \text{kCal / g} \times \text{Crude protein} + (9\ \text{kCal / g} \times \text{Crude fat}) + \left(4\frac{\text{kCal}}{\text{g}} \times \text{Carbohydrate}\right) \tag{6}$$

2.2.5. *Carbohydrate availability evaluation*

The carbohydrate contents of the samples were measured using an in-house method (no. STP/Chem/A03, which follows the principles of food analysis from the 2nd sub-component, as outlined by Kumar and Aalbersberg (2006). Available carbohydrates (CHO) were calculated using equation [5]:

$$\text{AvailableCHO}'\text{s}\left(\frac{\text{g}}{100\text{g}}\right) = 100 - \{[\text{Ash}] + [\text{Moisture}] + [\text{Fat}] + [\text{Protein}] + [\text{Dietary fiber}]\} \tag{5}$$

To calculate carbohydrate content, the percentages of moisture, ash, fat, protein, and fiber were subtracted from 100. This calculation helps determine the proportion of carbohydrates present in the sample.

2.2.6. *Reduce sugar content*

The in-house method STP/Chem/A10 was employed to analyze the reduced sugar profile following the principles of AOAC 967.21–16th Ed (Dubois *et al.*, 1956). To use this method, mix 0.34 g of potassium ferricyanide, 5 g of potassium cyanide, and 20 g of sodium carbonate with 1 liter of water. Next, approximately 0.1 mL of a 1.0% sample solution is combined with a reagent mixture (4.0 mL). The mixture was heated in a boiling water bath for 10 min prior to cooling. The absorbance of the solution was measured at nm wavelength of 420. To complete the process, sugar concentration curves were plotted against absorbance values. These curves can be used to calculate the arabinose content, which helps determine the reduced sugar profile.

2.2.7. *Energy evaluation*

To evaluate the potential energy content of the food, the approach described in Pearson's chemical analysis of foods (6th Ed., page 578) was employed, referred to as the in-house method No. STP/Chem/A01. Gross energy content was computed based on carbohydrate (CHO), crude fat, and crude protein levels. This calculation was performed using the mathematical equation [6]

To calculate the energy content (kCal/g), the protein, fat, and carbohydrate contents were multiplied by energy values of 4, 9, and 4 kCal/g, respectively. This calculation provides an estimation of the potential energy present in food.

2.2.8. *Crude fiber evaluation*

To determine the crude fiber content in the samples, we followed the AOAC 16th Edition method 962.409 using the in-house method STP/Chem/A08 (AOAC, 2000). To conduct this analysis, 600 mL tall-form beakers were used. Beakers were used to prepare the filtrate and washing with water was performed to estimate the total volume of the solution. The combined solutions were weighed. Next, the process included the addition of 4 times the volume of 95% ethanol (EtOH) preheated to 60°C. The 60% ethanol fraction was used to clean the filter flasks. Deionized water was introduced into the mixture of the filtrate and water-washing solution at 60°C to regulate the weight and increase it to 80°C. This process was conducted to determine the crude fiber content of the samples using a specified method.

2.3. *Statistical analysis*

The observed data were subjected to statistical analysis using Minitab®21.2 version. Using Fisher's method, the average and standard deviation (SDs) of each sample were calculated to compare the results. A significance ($p \leq 0.05$) level was used as a threshold to identify significant differences between the various samples. This analysis aimed to

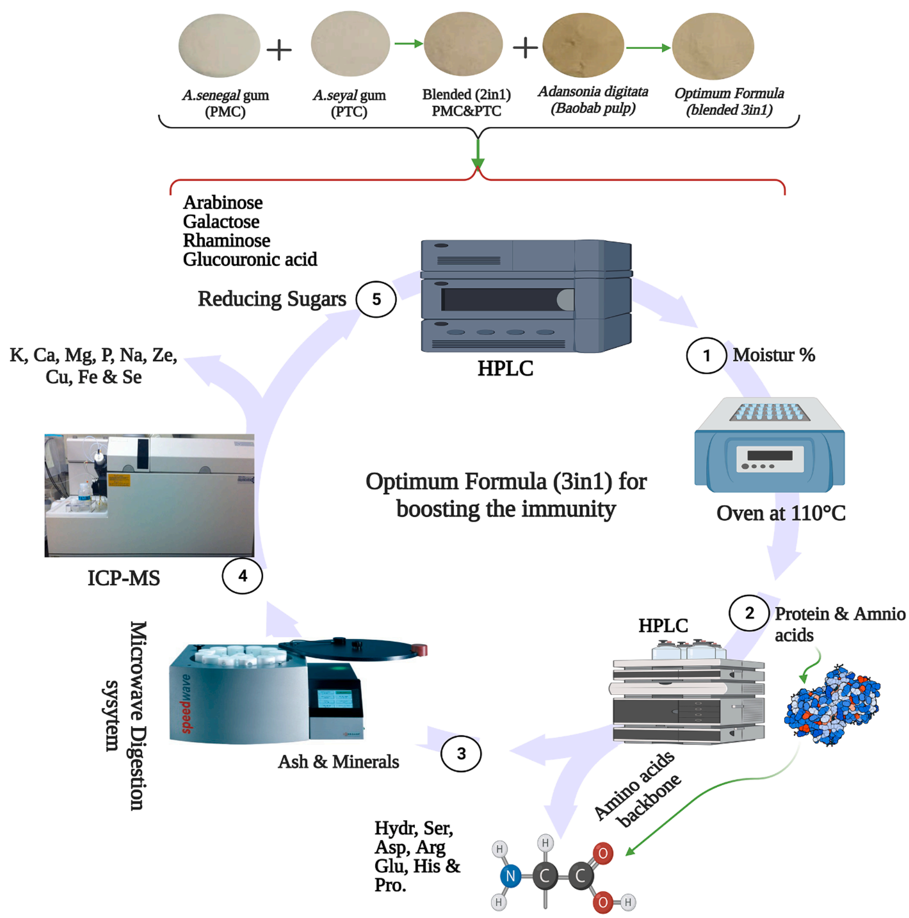

Fig. 1. Graphical illustration of the practical procedure for achieving a precise optimum blended formula. The optimum formula was blended in a specific ratio of 5:3:2 comprising *A. senegal* gum (PTC), *A. seyal* gum (PMC), and ADLP, respectively, to adequately evaluate the nutritional status of naturally supporting HIIs to treat infected Covid-19 asymptomatic patients. The color and distinctive shape of the optimum formula are accurately depicted.

provide insights and conclusions based on the collected data.

3. Results and Discussion

3.1. Determination of nutritional value

A diverse array of nutrients was meticulously examined and gauged to determine the nutritional value of the optimal formula. This involves the evaluation of carbohydrates, proteins, fats, vitamins, and minerals to acquire new perspectives on the health advantages and optimal consumption methods of the product. We investigated the physical, chemical, and biological attributes of the 3 in1 formulas (*A. senegal, A. seyal*, and ADLP), and the results in Tables 1-4. This study was conducted as outlined in Fig 1.

3.2. Physicochemical properties of the optimal blended formula

3.2.1. Proximate values (PVs)

Calculating PVs is crucial for evaluating macronutrients and other constituents in food and feed samples (Wang *et al.*, 2023b). Table 1 displays the PVs of the 3 in1 blended samples that are currently under investigation. Interestingly, the PVs of the *A. senegal* and *A. seyal* blends within the 2 in1 mixture closely resembled those of the blended 1 in1 ADLP sample. In general, all 3 samples displayed significant nutritional value. To be more specific, the energy content of the blended 2 in1 sample was recorded at 340.67 kcal/100 g, while the blended 1 in1 ADLP sample showed a slightly higher value of 350.12 kcal/100 g. Consistent with the study by Eke *et al.* (2013b), the blended 1 in1 ADLP sample demonstrated energy values spanning from 282.03 to 454.11 kcal/100 g. Analysis of Variance (ANOVA) revealed a significant difference ($p \leq 0.05$) between the 3 in1 and 2 in1 blended samples. The three samples exhibited notable variability in their nutritional characteristics.

3.2.2. Moisture and ash content

Moisture content analysis was performed to quantify the water and volatile compounds. However, ash content analysis revealed that the inorganic residue remained after thorough combustion (Li *et al.*, 2023a). This residue provided valuable information regarding the mineral composition of the substance. In the blended 3 in1, 2 in1, and 1 in1 samples, the moisture content ranged from 10.57% to 11.50%. Notably, the blended 3 in1 sample had a moisture content of 11%, whereas the blended 2 in1 sample had a higher moisture content of 11.5% (Table 1). In comparison, Ali, and Daffalla (2018) and Lelon *et al.* (2010) reported higher mean moisture values of 14.5% and 15.2% for *A. senegal* and *A. seyal* (2 in1), respectively. In contrast, Aluko *et al.* reported relatively similar mean values for the moisture content, which decreased from 9.16% to 10.30% (2018). Statistical analysis showed a significant difference ($p \leq 0.05$) in the moisture content among the various formulas. Notably, the moisture content of *A. senegal* and *A. seyal* (2 in1) fell within the internationally accepted range of 13–15%. The average ash contents of the 1:1, 2:1, and 3:1 blends were 3.48, 4.0, and 4.5%, respectively (Table 1). The values reported by Lelon *et al.* (2010) for *A. senegal* and *A. seyal* (2 in1) surpassed the effective mean of 2.5% reported by Ali and Daffalla (2018). The formula and blending processes affected the ash content and caused significant variation ($p \leq 0.05$).

Consequently, the blending process notably affects the moisture and ash content, impacting the nutritional value and standard compliance.

3.2.3. Dietary fibers (DFs)

DFs, which consist of soluble and insoluble carbohydrates that resist digestion, play a pivotal role (Li *et al.*, 2023c). In this study, the blend of 3 in1 aqueous solution exhibited the highest DF content (57%). In contrast, the blended 2 in1 and 1 in1 ADLP samples exhibited lower values of 1.865 and 48%, respectively (Table 1). Notably, both *A. senegal* and *A. seyal* (2 in1) had 85% soluble dietary fiber (SDF), as documented by Mariod *et al.* (2018). Interestingly, these values surpass those reported by Gadour *et al.* (2017) for the blended 1 in 1 ADLP sample by approximately 6%. The levels of soluble IDF and IDF varied significantly ($p \leq 0.05$) among the samples, with blend 3 in1 having the highest content. Inflammation can be reduced, and the immune response to Covid-19 is boosted by DFs and prebiotics (Hajipour *et al.*, 2022). Therefore, varying the DF concentrations in blends significantly affected their potential to reduce inflammation and boost immune responses against Covid-19.

3.2.4. Polysaccharides and carbohydrate content

Carbohydrate content refers to the amount of carbohydrate in a food or substance. Polysaccharides are complex carbohydrates characterized by the formation of multiple sugar units (BeMiller, 2018). In this study, we detected prebiotic polysaccharides (PPs) in all blended samples. The blended 3 in1 sample had a median value of 88.61%, whereas that of the blended 2 in1 sample was only 84% (Table 1). Xiao et al (2024) discovered that polysaccharides can exert therapeutic effects in patients with mild Covid-19 by cleansing their lungs. Chen et al (2020b) delved into the potential of polysaccharide consumption in preventing and treating Pulmonary Fibrosis (PFs). Polysaccharides have numerous benefits for respiratory health and these studies have contributed to our knowledge.

The samples displayed a spectrum of carbohydrate content values from 78.40% to 86.32%. These values exhibited statistically significant variations in the carbohydrate content among the 3 samples ($p \leq 0.05$). In particular, the blended 1 in 1 ADLP samples had a carbohydrate content of 78.40% (Table 1). In contrast, the blended 2 in1 sample exhibited a carbohydrate content of 84.34%, which was significantly lower ($p \leq 0.05$) than the remarkable 86.32% observed for the blended 3 in1 sample. Gurashi *et al.* (2016) reported a carbohydrate content of 62.58% for the blended 1:1 ADLP sample, influenced by factors like fruit form, type, and location. The components of this formula exhibit unique chemical properties that function simultaneously. Scientists have studied the effect of the SARS-CoV-2 spike protein on Covid-19 treatment and prevention (Luo *et al.*, 2020a; Robles *et al.*, 2022; Vankadari and Wilce, 2020; Woo *et al.*, 2020; Yang *et al.*, 2020b; Zhou *et al.*, 2022). These research endeavors have contributed to an evolving understanding of the intricate interactions between biochemical compounds and health outcomes.

Schirinzi *et al.* revealed that individuals with Covid-19 exhibited increased levels of human epididymis and carbohydrate antigens (CA-125) (2020). Additionally, the study found that the S1 domain of the Covid-19 spike protein interacts with CD26, which plays a role in the ability of the virus to invade and its virulence (Drzymała, 2024; Scheim, 2022). Previous studies have extensively investigated the beneficial effects of carbohydrates (CHOs) in individuals with Metabolic Syndrome (MeT-S) (Akter *et al.*, 2022; Clemente-Suárez *et al.*, 2022). Kim *et al.*, (2020) found that molecules that recognize carbohydrates can affect virus evolution toward infecting specific hosts. In COVID-19, the consumption of CHOs resulted in a 92% improvement in the health of infected athletes, as recently reported by several scholars (Pavlidou *et al.*, 2024; Pirani *et al.*, 2023; Sharma, 2024). Therefore, varying DF concentrations in blends significantly affected their potential to reduce inflammation and boost immune responses against COVID-19.The potential vulnerability of individuals to SARS-CoV-2 infection may be influenced by the interaction of carbohydrates (CHOs) with sialic acid receptors on host cells (Aloor *et al.*, 2022; Díaz-Salinas *et al.*, 2024). According to recent studies, the receptor-binding domain of SARS-CoV-2 spike proteins appears to have a preference for recognizing blood group A antigens, which may affect disease susceptibility (Boavantura *et al.*, 2023; Wu *et al.*, 2023). According to previous research, individuals with blood group A may be more susceptible to Covid-19 due to the presence of natural anti-blood group antibodies (Boavantura *et al.*, 2023; Wu *et al.*, 2023). This conclusion is based on studies exploring the association between ABO blood groups and Covid-19 susceptibility (Al Sulaiman *et al.*, 2024). In addition, the interaction of SARS-CoV-2 with sialic acids on host cells is vital for viral infection and transmission, as it influences the ability of the virus to attach to the host cells (Saso *et al.*, 2022). Therefore, recognizing the significance of these molecular connections is crucial to uncover the processes of viral entry and disease progression in the context of COVID-19.

According to Lin *et al.*(2022), Vaccination against Covid-19 is vitalfor fortifyingy the immune system andpreventingt life-threatening situations. Studies have revealed that individuals possessing greater knowledge of Covid-19 vaccines commonly exhibit more favorable attitudes toward vaccination (Sonmezer *et al.*, 2022). Furthermore, lifestyle factors such as physical fitness can bolster the capacity to tolerate adverse effects of vaccines and improve the quality of vaccination practices (Miao *et al.*, 2022). Furthermore, the immune response generated by vaccines, including antibody production and T-cell activation, is crucial for controlling Covid-19 infection (Sun et al., 2023). Incorporating complex carbohydrates into one's diet alongside Covid-19 vaccination may offer a comprehensive approach to enhance the immune system and reduce the likelihood of severe outcomes (Cundra *et al.*, 2023). This study suggests a formula that can be used as a superfood supplement to treat viral infections during epidemics. However, it is imperative to investigate the intricacies of the carbohydrate phenomenon in Covid-19 (Jang et al., 2024; Morniroli, 2024; Xiao et al., 2024). Thus, there is a need to explore and understand how carbohydrates interact with the global health crisis.

3.2.5. Protein composition

Examination of the protein composition revealed that the blended 3 in1 sample exhibited a protein content of 3.34%. This determination was based on the type and quantity of individual amino acids within the protein structure. In contrast, the protein content in the 2in1 and 1in1 blended samples was slightly lower (2.36% and 2.50%, respectively). The findings indicate a significant difference in the average protein content between the blended 3in1 sample, with values of 2.4% and 3.34%, respectively, with a significant difference ($p \leq 0.05$). Multiple studies have reported protein values for *A. senegal* and *A. seyal* ranging from 1.3% to 3.0% (Ahmed *et al.*, 2018; Ali and Daffalla, 2018; Dawkins and Nnanna, 1995; Elnour, 2007; Karamalla, 1965; Karamalla *et al.*, 1998; MK *et al.*, 2008; Siddig, 1996; Yebeyen *et al.*, 2009). Aluko *et al.* (2016) found that ADLP from 3 Tanzanian sites displayed a protein content ranging between 3.23% and 3.53%, which was higher than the 3.5% reported by Oyeleke *et al.*(2012). Thus, the 3 in1 blend exhibited a notably higher protein content than the 2 in1 and 1 in1 samples, reflecting the variability in protein levels across similar botanical products.

Jones *et al.* found that proteins play a crucial role in Calcium Channel Blocking (CCB), which can help suppress harmful substances in the body (2024). The authors studied 600 enzymatic reactions, including those related to the Covid-19 immune and inflammatory responses (Belchior-Bezerra *et al.*, 2022; Di Flora *et al.*, 2023). This observation highlights the importance of proteins in controlling kidney potassium loss and in supporting the function of vitamin D (Skalny *et al.*, 2023). Proteins have the potential to greatly affect individuals with weakened immune systems and are infected with Covid-19 (Di Flora *et al.*, 2023). In instances of severe infection, it is believed that pro-inflammatory cytokines such as IL-1, IL-6, IL-12, IFN-γ, and TNF-α may worsen an individual's condition (Mińko *et al.*, 2024). Individuals with compromised immune systems, such as those with hematological malignancies, may not receive the same level of protection from Covid-19 through vaccination as individuals with stronger immune systems (Suribhatla et al., 2023). These findings emphasize the need to understand the interplay between proteins and immune responses in individuals with weakened immune systems who are battling Covid-19.

3.2.6. Fat and cholesterol levels

Fat content quantifies the quantity of lipids in food, whereas cholesterol content indicates the amount of cholesterol within the same food (Martins *et al.*, 2023). Cholesterol levels can affect cardiovascular health. The 3 in1 sample (Table 1) had more fat and cholesterol (0.30%) than the 2 in 1 sample (0.0133%). The blended 1 in 1 ADLP sample had an average fat value of 0.30%, according to Osman (2004). Oyeleke *et al.* (2012) found that fat content ranged from 0.4% to 1.70%. The fat and cholesterol levels of all the samples exhibited a consistent trend, except for the 2 in1 blended sample, which contained no fat or cholesterol. These findings show the nutrients in the mixed samples and how they might affect heart health.

The link between obesity, Covid-19, and innate immunometabolism has been previously investigated (Kumar, 2021; Matveeva *et al.*, 2022). Meta-flammarion, a factor associated with obesity, increases the host's reaction to a new viral pathogen. Individuals with obesity or diabetes who need prolonged ventilation are advised to take low-DFA food supplements as per researchers (Aksoy *et al.*, 2020; Al-Benna, 2020; Alessi *et al.*, 2020; Onishi *et al.*, 2020). Thus, people with health issues, particularly during the Covid-19 pandemic, may find health advice and nutritional support to be helpful.

Difructose dianhydride (DFAs) can lower Covid-19 mortality in people with MeT-S Covid-19 targets several aspects, including cytokine storm, lungs, and intestines (Li *et al.*, 2023a). DFAs have been demonstrated to enhance intestinal functions such as calcium absorption and barrier function preservation (Lee and Kim, 2018). Understanding the physiological systems impacted by DFAs could offer valuable insights into their potential to reduce severe outcomes in Covid-19 patients (Li *et al.*, 2023a). Prior research has shown that DFAs promote calcium and iron absorption in the intestine, which influences the cecal mucosa and maintains DMT-1 mRNA expression (Mortada *et al.*, 2023). The consumption of DFAs has also been linked to increased intestinal permeability (Inczefi *et al.*, 2022). The blended 3 in1 formula comprising *A. senegal, A. seyal,* and ADLP offers another avenue for enhancing Host Immune Interaction (HII) levels. Solutions containing 1 in1 ADLPs can improve health by reducing inflammation and promoting weight loss (Cicolari *et al.*, 2020; Suliman *et al.*, 2020). To effectively combat Covid-19, further research on blending technology is warranted (Lee and Hong, 2024). This study helps boost the immune response of people with weakened immune systems, which is essential for fighting pandemics (Cámara et al., 2021). Blending techniques can improve the health of people at a high risk of severe Covid-19 infection.

Table 2
Mineral's profile of the optimal 3 in1 formula comprising *A. seyal* and *A. senegal* gum (PMC and PTC) powder and ADLP powder.

Metals	PMC&PTC (Blended 2in1) Mean ± S.D	ADLPs	Optimum formula (Blended 3in1)
Calcium	(g/100gDW) $0.9343.0\pm0.0200^{c}$	(g/100gDW) 68.20 ± 2.50^{c}	(g/100gDW) 68.54 ± 3.12^{b}
Potassium	$0.2359.02\pm0.050^{c}$	70.22 ± 4.30^{b}	70.56 ± 2.35^{a}
Magnesium	$0.1654.01\pm0.0300^{c}$	16.52 ± 4.80^{b}	16.60 ± 4.80^{a}
Phosphorus	0.0301 ± 0.00100^{c}	11.50 ± 2.500^{a}	$11.50.00\pm3.70^{a}$
Sodium	0.0408 ± 0.00100^{b}	31.90 ± 1.200^{a}	31.40 ± 4.80^{a}
Zinc	0.000122^{c}	1.8 ± 0.11000^{b}	$1.9.00\pm0.14^{a}$
Copper	0.000116^{c}	1.6 ± 0.10130^{b}	19.19 ± 2.100^{a}
Iron	0.000122^{c}	9.3 ± 1.14200^{b}	15.12 ± 1.812^{a}
Selenium	0.000004^{c}	0.036 ± 0.005^{a}	0.037 ± 0.005^{a}
Mercury	0.0000028^{c}	0.05 ± 0.0020^{a}	0.050 ± 0.005^{a}
Arsenic	0.0000020^{c}	0.015 ± 0.002^{a}	0.011 ± 0.003^{a}
Lead	0.000001^{c}	0.02 ± 0.0120^{a}	0.02 ± 0.012^{a}
Cadmium	N.D.	0.0133 ± 0.003^{a}	0.0113 ± 0.002^{ab}
Antimony	N.D.	0.0123 ± 0.001^{a}	0.0123 ± 0.004^{a}
Tin	N.D.	0.040 ± 0.0020^{a}	0.040 ± 0.001^{a}

Note: * Mean value ± SD in raw, followed by different superscript letters indicates a significant difference ($p\leq0.05$) between rows. **PMC**, *A. senegal* gum (commercial); **PTC**, *A. seyal* gum (commercial); **ADLP**, *A. digitata* pulp powder; **ND, not detected**.

3.3. Evaluation of mineral content of the optimum formula

The presence of minerals is critical for determining the inorganic features of a substance (Godswill *et al.*, 2020). As illustrated in Table 2, the blends of 2 in1, 1 in1, and 3 in1 exhibit distinct mineral compositions. Different factors, such as the type of sample, blending ratio, and method, affected the mineral content of all the samples (Table 2). A significant observation was that the blended 3 in1 sample exhibited notably higher levels of specific minerals, including calcium (Ca), potassium (K), magnesium (Mg), phosphorus (P), and sodium (Na), compared to the other samples, with a statistical significance of ($p\leq0.05$). This difference shows how mineral composition affects the final mineral content based on the blending ratio.

3.3.1. Calcium content

Calcium is crucial for maintaining bone and muscle strength. We determined the calcium levels in foods and beverages (Shkembi and Huppertz, 2021). Based on the findings of this study, the calcium concentrations in the 2 in1, 1 in1, and 3 in1 blended samples were 0.9343, 68.20, and 68.54 g/100 gDW, respectively (Table 2). The calcium levels in *A. senegal* and *A. seyal* (2 in1) were moderately higher, according to Yebeyen *et al.* (2009), whereas blended ADLP had lower levels in studies by Muthai *et al.* (2017a) and Stadlmayr et al. (2020). Studies have shown that calcium can block ion channels in Covid-19 patients, which may affect cell function (Sultan *et al.*, 2022). This observation was confirmed in a study by Jayaseelan and Paramasivam (2020), whereas Sun *et al.* (2020) identified a significant association between CCBs and Covid-19 treatment. The severity and prognosis of Covid-19 are linked to calcium levels, which highlights the importance of their management.

3.3.2. Potassium content

The average potassium concentration in the blended 3 in1 sample was significantly higher, measuring at 70.56 g/100 gDW, in contrast to 70.22g/100 g DW in the blended 1 in1 ADLP sample (without gum). The differences were statistically significant ($p\leq0.05$). Conversely, the K concentration in the blended 2 in1 sample was considerably lower than the average concentration (0.2359 g/100 g DW). When analyzing pure blended 1 in 1 ADLP samples, previous studies conducted by Stadlmayr *et al.* (2020), Abdullahi *et al.* (2014), and Eke *et al.* (2013a) reported lower mean potassium concentrations, which were recorded as 1.00g/100 gDW, 0.240g/100 gDW, and 0.125g/100 gDW, respectively. The potassium content showed distinct variations from other minerals in this study, which can be attributed to various factors including geographical location, quantification methodologies, and blending processes (He *et al.*, 2023). These variances underscore the intricacies in determining mineral concentrations and highlight the multifaceted nature of the factors that influence these measurements. In this context, Chen *et al.* (2020a) demonstrated that including organic bioactive compounds within a 3 in1 formula positively affects the potassium (K) content of Covid-19. Thus, the 3 in1 blend showed notably higher potassium levels, influenced by blending processes and other factors affecting mineral content.

A case-control study conducted across multiple countries revealed a strong relationship between hypokalemia and renal potassium loss, which may be attributed to the degradation of Angiotensin-Converting Enzyme 2 (ACE2), a crucial enzyme associated with severe acute respiratory syndrome (Wieërs *et al.*, 2022). The severity of hypokalemia can be influenced by a combination of intestinal loss and reduced renal potassium preservation (Bamgbola, 2022). Hypokalemia, which frequently appears in different clinical presentations, can result from several factors including potassium(K+) deficiency due to dietary limitations, vomiting, or excessive loss through the kidneys (Huang *et al.*, 2020c). Distal potassium secretion can be stimulated, which activates the renin-angiotensin-aldosterone system, resulting in sodium loss and a subsequent increase (Pearce *et al.*, 2022). Furthermore, hypokalemia may result from renal or gastrointestinal deficits, insufficient dietary intake, or shifts in intracellular distribution (Tavares *et al.*, 2022). Potassium (K+) consumption is recommended for individuals affected by Covid-19, with potential benefits in managing their condition (Okoloekwe *et al.*, 2023).

Shrivastava *et al.* evaluated various therapeutic agents that focus on immune transfer factors (2022). Their findings indicate that elements such as potassium (K), zinc (Zn), and selenium (Se), along with compounds such as ascorbic acid, vitamin E, and ferulic acid, play a role in both preventing and improving Covid-19 symptoms (Srivastava *et al.*, 2022). This underscores the potential importance of these nutrients and compounds in supporting immune responses and overall health during Covid-19 infection.

3.3.3. Magnesium content

The magnesium content refers to the amount of magnesium present in foods and beverages, as examined in a study conducted by Trapani *et al.* (2022b). Table 2 shows that the 3 in1 sample had 16.60 g magnesium per 100 g DW, which was higher than that of the 1 in1 sample (without gum) with 16.52 g. In contrast, the blended 2 in1 sample displayed the lowest average magnesium content among the blended samples, measuring 0.1654 g/100 g DW. Yebeyen *et al.*(2009) reported a notably higher Mg value of 0.201 g/100 g DW for *A. senegal* and *A. seyal* (2 in1), which was twice as high. For blended 1 in1 ADLP, Muthai *et al.* (2017a) and Eke *et al.* (2013a) reported magnesium values of 0.23 g/100 g DW and 0.019 g/100 g DW, respectively. Magnesium deficiency is linked to certain pathogenic factors in Covid-19 patients (Coman *et al.*, 2023; Guerrero-Romero *et al.*, 2023; Trapani *et al.*, 2022a). This observation aligns with recent research findings that indicate that trace elements present in functional foods, including magnesium (Mg), zinc (Zn), iron (Fe), selenium (Se), and copper (Cu) derivatives, may confer protection against viral respiratory infections, including the Covid-19 virus (Alkhatib, 2020; Mitra *et al.*, 2022; Ricci and Roviello, 2023). Therefore, the higher Mg content in the 3in1 blend could enhance the protection against Covid-19 by managing pathogenic factors.

3.3.4. Phosphorus content

Mineral phosphorus plays a crucial role in facilitating the growth, maintenance, and restoration of bodily tissues, and contributes to bone and tooth development (Molenda and Kolmas, 2023; Shapiro and Landis, 2024). Regarding the phosphorus (P) content in this study, the blended 3 in1 and 1 in1 ADLP samples exhibited similar phosphorus levels, with an average of 11.50g/100 gDW. In contrast, the blended 2 in1 sample demonstrated a notably lower average phosphorus content, measuring only 0.0301 g/100 g DW. The results of this study, which involved analyzing the ANOVA results between blended and non-blended samples, provided a deeper understanding of the variations in phosphorus levels among different sample types. In contrast, Yebeyen *et al.*, (2009), Kinuthia (2018) presented markedly different findings, reporting a significantly ($p \leq 0.05$) lower mean of phosphorus 0.11g/100 gDW for the blended 1 in1 ADLP sample compared to the average p-value of 0.6 g/100 gDW for *A. senegal* and *A. seyal.* Inconsistent results from prior experiments highlight the limitations of the titration method in comparison with advanced instrumental techniques, such as ICP-MS. The heightened accuracy of ICP-MS makes it particularly promising for future research, and potentially serves as a benchmark for blended technologies. Remdesivir has been separated from diastereomers using phosphorus and Pseudomonas diminuta (Jaito *et al.*, 2024; Vargas *et al.*, 2021).

3.3.5. Sodium content

The essential role of sodium in maintaining fluid balance, blood pressure, and nerve and muscle function has been highlighted by several researchers (Bernal *et al.*, 2023; Chrysohoou *et al.*, 2022; Jhee *et al.*, 2022; Martin *et al.*, 2023; Shin and Lee, 2021). The results of this study indicate that the average sodium (Na) content in the blended 3in1 and 1in1 ADLP samples was comparable, with measurements of 31.4 and 31.90g/100gDW, respectively. Conversely, the blended 2 in1 sample showed a significantly lower average sodium (Na) value (0.0408 g/100 g DW) ($p \leq 0.05$). Statistical analysis showed that the sodium contents of the blended and unblended samples were significantly different ($p \leq 0.05$). Consistent with the findings of Kinuthia (2018) and Yebeyen *et al.* (2009), the sodium concentrations for *A. senegal* and *A. seyal* (2in1), respectively, were reported as 0.1 g/100g DW for the blended 1:5 ADLP sample and 0.01g/100gDW for the blended 1:5 ADLP sample. Tan *et al.* demonstrated an association between sodium intake and mortality rate in China (2022). High sodium intake has been linked to lower mortality rates in Covid-19 patients in China than in other countries (Luo *et al.*, 2020b; Zhang *et al.*, 2021). There is a need for further research on sodium profiling, with ICP-MS being preferred over the titration methods.

3.3.6. Trace elements

Trace elements are chemical elements that are crucial for the proper functioning and growth of living organisms, although they are required in relatively small quantities (Islam et al., 2023). In this study, we examined the concentrations of crucial trace elements, including copper (Cu), Iron (Fe), Zinc (Zn), and selenium (Se), at 19.19, 15.12, 1.9, and 0.0037 g/100 g DW. Interestingly, the blended 3 in1 sample did not show any detectable trace elements compared to the blended 2 in1 sample (Table 2). Trace element levels were different ($p \leq 0.05$) in the 2 blended samples, similar to Yebeyen *et al.* (2009) study that found trace element values at 0.001g/100gDW and no traces of Zn, Cu, Pb, Cd, Co, Ni, Mn, and Cr. It is important to consider the trace element composition to assess the nutritional quality of the blended samples.

These findings support the idea that combining *A. senegal, A. seyal*, and ADLP can boost the immune response to combat COVID-19. When formulating an ideal blend and conducting experiments, it is of utmost importance to ensure that the levels of heavy metals comply with the safety standards established by regulatory bodies such as the US Food and Drug Administration. This ensured that the final product was safe for consumption. The blended formula developed in this study aligns with the trace element levels specified by the Food and Drug Administration (FDA) standard requirements reported by Talebi *et al.* (2019). Specific metal values are presented in Table 2. The integration of selenium (Se) with other micronutrients, such as vitamins C and E, Zinc, copper, iron, and cysteine, has been shown to protect against Covid-19, as observed in previous studies (Batiha *et al.*, 2022; Engin *et al.*, 2022; Kumar *et al.*, 2024). This emphasizes the potential of the blended formula to contribute to immune defense against the virus.

Martinez *et al.* (2022) highlighted the influence of trace elements on immune function in individuals with low selenium levels, particularly poliovirus. In support of this, Sun *et al.* demonstrated that selenium intake, especially in individuals with marginal selenium status, enhances immune activity against poliovirus(2023b). These mechanisms encompass the formation of sodium selenite (Na_2SeO_3) from pharmacological preparations of selenium under high blood selenium levels, which thwarts virus-cell interactions. Selenium in selenoproteins contributes to influenza virus mutations (Rayman *et al.*, 2023). Deficiency exacerbates influenza-related pathology and increases the susceptibility to, and severity of, viral RNA infections (Moghaddam et al., 2020). This collective evidence underscores the crucial role of selenium in fortifying immune responses, its potential in addressing viral infections such as

Covid-19, and its implications for broader health concerns.

Jayawardena *et al.*, (2020) and Razzaque (2020) both noted a significant improvement in immune response in elderly individuals through oral zinc supplementation. This trend was also reflected in the in vivo study by Barnett *et al.* (2016), which involved a three-month supplementation with 30 mg of zinc in elderly nursing home residents (NHEC). Despite this, not all deficient NHECs reached sufficient zinc levels; however, elevated serum zinc concentrations were correlated with improved T-cell functionality and quantity. Several studies have confirmed that zinc supplementation is linked to a decrease in the levels of pro-inflammatory cytokines, such as IL-6 and IL-1, and an increase in the production of type I interferon, which may be beneficial in managing Covid-19 infections (Almeida Brasiel, 2020; Dhawan *et al.*, 2022). Research has demonstrated that zinc supplementation may decrease the intensity and duration of cold symptoms, which could potentially include symptoms associated with Covid-19 (Sharif *et al.*, 2022). The promising potential of zinc in improving immune function in Covid-19 patients lies in its antiviral properties and capacity to regulate immune and inflammatory responses (Ishida, 2020). In addition, zinc supplementation has been associated with reduced death rates among individuals infected with Covid-19 (Olczak-Pruc *et al.*, 2022). Overall, evidence suggests that zinc supplements could serve as anti-inflammatory agents and enhance the immune function in individuals with Covid-19. The mineral profiles used in this study are presented in Table 2.

3.4. Evaluation of protein content and AAs in the optimum formula

Proteins are important components of the human body, and are composed of amino acids, carboxylic acids, and side chains. Twenty different proteins help to build tissue, repair, and catalyze biochemical reactions. These chains are constructed from amino acids. Table 3 displays the amino acid compositions of the different samples, revealing that the blending process and sample type had an impact. Remarkably, the blended 3in1 sample contained 96.27g of Essential amino acids (EAAs), markedly surpassing ($p \leq 0.5$) the blended 1 in1 ADLP (31.41 g/100 g DW) and 2 in1 (42.11g/100 g DW) samples. Meanwhile, Non-EAAs (NEAAs) tallied 32.16g/100 g DW for the blended 2 in1, 51.63 g/100 g DW for the 1 in1 ADLP, and 85.07g/100 gDW for the 3 in1 sample.

Table 3
The AA composition of the optimal 3in1 formula comprises *A. seyal* and *A. senegal* gum (PMC and PTC) powder and *A. digitata pulp* (ADLP) powder.

Amino acid	PMC&PTC (Blended 2in 1) Mean ± S.D	ADLPs	Optimum formula (Blended3in1)
	(g/100gDW)	(g/100gDW)	(g/100gDW)
Hydroxyproline	22.07±0.513^{b}	N.D.	30.17±0.122^{a}
Histidine	2.30±0.608^{hij}	2.23±0.058^{uvw}	13.50±0.71^{gh}
Isoleucine	1.57±0.321^{wxy}	2.23±0.057^{uvw}	3.77±0.150st
Leucine	7.17±0.577^{jkl}	4.37±0.116^{qrst}	12.4±0.460^{gh}
Lysine	2.60±0.346^{t}	1.73±0.058^{vwx}	3.80±0.100st
Cysteine	N.D.	0.90±0.100^{yzaa}	0.95±0.012^{yzaa}
Methionine	0.11±0.010^{za}	0.197±0.006^{za}	0.32±0.020^{za}
Tyrosine	1.80±0.100^{vwxy}	7.70±0.173^{klmno}	9.50.43±0.40^{f}
Phenylalanine	1.83±0.056 ^{vwxy}	4.53±0.231^{pqrst}	8.27±0.21^{klmn}
Threonine	1.80±0.1001 ^{vwxy}	2.70±0.17st	8.7±0.52^{klm}
Valine	2.93±0.058^{pqrst}	4.83±0.057^{pqrst}	9.47±0.35^{ijk}
Total EAA	**44.18**	**31.41**	**96.27**
Arginine	1.33±0.058^{xyz}	7.70±0.17^{klmno}	14.44±0.15 ^{ef}
Glutamine	5.43±0.404$^{\circ pqrst}$	6.60±0.17^{mnopq}	11.31±0.29^{hij}
Asparagine	9.40±0.265 ^{jk}	6.43±0.058^{mnopqr}	14.83±0.14^{ef}
Proline	11.23±0.58 ^{hij}	2.370±0.38 ^{t}	11.87±0.81^{hi}
Serine	16.57±0.57^{d}	3.37±0.29st	18.45±0.44^{ec}
Alanine	4.10±0.17rs^{t}	3.47±0.29st	7.67±0.19^{klmno}
Glycine	3.57±0.115st	2.667±0.41^{t}	6.50±0.25^{nopqr}
Total NEAA	**51.63**	**32.16**	**80.87**

Note: * Mean value ± SD in raw, followed by different superscript letters indicates a significant difference ($p \leq 0.05$) between rows. **PMC**, *A. senegal* gum (commercial); **PTC**, *A. seyal* gum (commercial); **ADLPs**, A. digitata pulp powder; **EAA**: Essential Amino Acids; **NEAA**: Non-essential Amino Acids.

3.4.1. Hydroxyproline and serine content

Hydroxyproline, a non-proteinogenic AA, is primarily present in collagen and indicates the collagen concentration. Conversely, serine, a polar AA that is widely distributed in proteins, is pivotal in the catalysis and regulation of protein activity. Compared to the other NEAAs, the blended 3 in1 sample had significantly more serine (18.45 g/100 g DW), according to the study ($p \leq 0.05$). In contrast, Ibrahim *et al.* (2016) reported a lower serine content of 3.37g/100 g DW in the blended 1 in1 ADLP sample. The blended 3 in1 sample registered a hydroxyproline content of 30.17g/100 gDW, surpassing the combined 2 in1 sample's hydroxyproline content of 22.07g/100 g DW. According to Wu *et al.* (2020). Hydroxyproline is typically not a significant component of plant-based foods even when blended in a 1:1 ratio. Hence, the 3 in1 blend had notably higher serine and hydroxyproline levels, indicating an enhanced collagen and protein functionality.

León de Pinto *et al.* (2002) highlighted that approximately 18% of the hydroxyproline, serine, and threonine content can be attributed to *A. senegal* and *A. seyal* gums. Consequently, blending *A. senegal* and *A. seyal* is crucial for obtaining the optimal formula (blend 3 in 1) enriched with these compounds. Hydroxyproline and serine, which act as antiviral agents, have significant potential in various applications (Umumararungu *et al.*, 2024). According to Mardi *et al.* (2023) hydroxyproline is crucial for reinforcing the immune system and for protecting against coronaviruses and other infectious diseases caused by fungi, bacteria, and parasites.

3.4.2. Asparagine and arginine content

Different active groups have been identified for asparagine and arginine. Asparagine has a carboxamide group, while arginine has a guanidino group. In the blended 3 in1 sample, asparagine and arginine were present at 14.44 g, categorized as essential “"NEAA"” in this study. The difference ($p \leq 0.05$) in NEAA levels between blended and non-blended samples was significant. The results show that the levels of arginine and asparagine fall within a range of 1.30 g/100 g DW to 9.40 g/100 g DW, which is similar to what Salem *et al.*, (2016) found in *A. senegal* and *A. seyal* (2 in1). These levels surpass the 6.30 g/100 g DW for asparagine and arginine, respectively, about the blended 1 in1 ADLP, as similarly observed in the outcomes of Ibrahim *et al.*, (2016). Therefore, the significant levels of asparagine and arginine in the 3 in1 blend indicate an enhanced amino acid content compared to both blended and non-blended samples.

Recent research has highlighted the vital role of arginine in fortifying the immune system and effectively managing a spectrum of metabolic syndromes including hypertension, peripheral artery disease, diabetes, and ischemic heart disease (Araujo *et al.*, 2022; Dou *et al.*, 2024; Pedrazini *et al.*, 2022; Zhao *et al.*, 2024). These findings are further supported by recent research that confirmed the significance of post-translational deamination mechanisms involving peptidyl arginine deiminases in the host response to SARS-CoV-2 and Covid-19 (Dey *et al.*, 2023; Malvankar *et al.*, 2023; Pasquero *et al.*, 2024; Pasquero *et al.*, 2023). Elevated arginine levels have been associated with immune status and airway remodeling in individuals with Covid-19 (Durante, 2022; Rahnavard *et al.*, 2022). According to previous research, arginine deficiency during the Covid-19 pandemic may result in coagulopathy, endothelial dysfunction, and abnormal T-cell regulation (Özbay *et al.*, 2023; Patil *et al.*, 2023; Shams *et al.*, 2022). The disruption of amino acid metabolic pathways, notably arginine metabolism, may be a targetable characteristic of severe Covid-19 (Haj *et al.*, 2022). Replenishing arginine and inhibiting arginase 1 have been proposed as potential approaches for preventing and treating Covid-19, according to suggestions made for these strategies (Dean *et al.*, 2021). Thus, maintaining sufficient arginine levels is essential for effective management of Covid-19.

3.4.3. Glutamine, histidine, and Proline

Amino AAs glutamine, histidine, and proline, possess distinctive side-chain characteristics, with glutamine featuring an amide functional group that is critical for enzymatic reactions and protein synthesis (Lewis *et al.*, 2024; Mirveis *et al.*, 2023; Zhu *et al.*, 2024). Histidine, with a positively charged side-chain, and proline, with a cyclic structure, are not involved in protein folding or structure, whereas positively charged side chains and proline, which have cyclic structures, are not involved in protein folding or structure (Al Mughram *et al.*, 2023). For the 3 in1 and 2 in1 blended samples, glutamine, histidine, and proline levels were similar at 11.28 g/100 g DW, with no statistically significant differences ($p \geq 0.05$). Corresponding mean values for *A. senegal, A. seyal*, and (2in1) were reported by Salem *et al.* (2016), while Ibrahim *et al.* (2016) reported similar results for the blended 1in1 ADLP, with histidine, proline, and glutamic acid levels of 2.14 g/100gDW, 7.94 g/100 g DW, and 12.23g/100gDW, respectively. This observation could explain the similarities in the AA profiles of different formulas. Notably, histidine and asparagine play crucial roles in the innate immune response against SARS-CoV-2 infection, and serve as antiviral targets for the inhibition of papain-like proteases (Plpro) in Covid-19 (Al-Shalan *et al.*, 2023; Saito *et al.*, 2024).

Indeed, research by Kukułowicz *et al.* (2024) and Hissen *et al.* (2023) provided evidence that various amino acids may modulate the immune response against Covid-19 by enhancing epithelial barriers, including proline, arginine, glycine, glutamine, taurine, and tryptophan. Similarly, M *et al.*, (2020) and (Khatri *et al.*, 2023) identified active binding sites such as serine-441, histidine-296, and aspartic acid-345, which are targeted by phytochemicals to inhibit Covid-19. Notably, glutamine supplementation during the early stages of Covid-19 has been linked to reduced ICU visits and shorter hospital stays, as highlighted by Cengiz *et al.* (2020) who demonstrated its immune-boosting effects by curbing inflammatory responses. Therefore, the findings of this study are significant because the proposed blended 3 in1 formula might offer valuable therapeutic benefits for infected patients with Covid-19 who are not immunocompromised.

3.4.4. Alanine, phenylalanine, and threonine

The EAA phenylalanine has an aromatic side-chain and is a precursor to dopamine and norepinephrine (Clifford *et al.*, 2024). At the same time, threonine, another EAA, features this enzyme synthesizes a hydroxyl group on its side, mucin, collagen, and proteins. In the blended 3 in1 sample, remarkable levels of alanine (7.67g/100 gDW), phenylalanine (8.27g/100 gDW), and threonine (8.70 g/100 g DW) were observed in the blended 3 in1 sample. In the blended ADLP sample, arginine content (7.70 g/100 g DW) did not differ significantly ($p \leq 0.05$) between the NEAAs and EAAs. According to Salem *et al.* (2016), phenylalanine, alanine, and threonine content in *A. senegal, A. seyal*, or (2 in1) are 3.80 g/100 g DW, 4.00 g/100 g DW, and 6.80 g/100 g DW, respectively. Notably, Aktas *et al.* (2020) in SARS-CoV-2, amino acids such as phenylalanine, glycine, tyrosine, and asparagine play important roles in the interaction between arbidol and spike glycoprotein-binding domains. Huang *et al.* (2020b) also explained these amino acids' functional role in arbidol's antiviral interactions.

Zhang *et al.* highlighted the role of threonine in suppressing cytokine storms and inflammation, mitigating pulmonary edema, and reducing fever in Covid-19 patients (2023). However, the presence of alanine may benefit patients with Covid-19 MeT-S by synergistically enhancing the host's immune response (Du Preez et al., 2022). Protein Kinase 1 (RIPK1), a primary mediator of inflammation-induced cell death, has been demonstrated in recent studies (Hao *et al.*, 2023; Shen *et al.*, 2023; Xu *et al.*, 2021). In patients with MeT-S, RIPK1 inhibition can cause kidney failure, stroke, myocardial infarction, and systemic inflammatory response syndrome (Xu *et al.*, 2024). Many antiviral drugs directly inhibit primary protease polymerase by interacting with amino acids including asparagine, cysteine, serine, leucine, threonine, and glutamine (Geromichalou *et al.*, 2022; Janin, 2024). Therefore, these amino acid groups contributed to the inhibition of Covid-19, highlighting the importance of formulations containing *A. senegal, A. seyal* gum, and ADLP.

3.4.5. Valine and leucine

The blended 2 in1 and 1 in1 ADLP samples contained similar levels of valine, measuring up to 4.67g/100 gDW. Valine is an amino acid essential for protein synthesis, energy generation, and tissue repair. Likewise, leucine, another EAA essential for muscle protein synthesis and energy production, was present in significant amounts in the blended 3 in1 sample (12.4g/100 gDW) compared to the blended 2 in1 and 1 in1 samples. Salem *et al.* (2016) they reported average valine and leucine values of 3.80, 4.90, and 9.50 mg/100g DW for *A. senegal and A. seyal* (2in1).

In contrast, Ibrahim *et al.* reported significantly higher values of 5.31 g/100 g DW for valine and 5.49 g/100 gDW for leucine (2016). Notably, the blended 1 in the 1 ADLP sample exhibited lower levels than the blended 3 in1 sample. Valine's potential role in preventing the conversion of alanine into valine by the human Amino Peptidase N-gene is noteworthy, as it prevents coronavirus binding by preserving a range of distinct domains essential for the attachment of the virus (Vijgen *et al.*, 2004). Valine's insoluble intercellular aggregation potential against Covid-19 development has also been established by Shi *et al.*, (2019). Thus, the 3 in1 blend had higher leucine levels and maintained the essential valine content, supporting muscle synthesis, energy production, and viral protection.

3.4.6. Glycine and phenylalanine

With its simple hydrogen side-chain, glycine plays a crucial role in collagen formation and connective tissue formation in the body. In contrast, phenylalanine serves as a precursor for neurotransmitters, such as norepinephrine and dopamine (Bose *et al.*, 2024; Gasmi *et al.*, 2022; Szigetvari *et al.*, 2023). The average value for the blended 2 in1 and 1 in1 ADLP samples was 3.65g/100 gDW, whereas the blended 3 in1 sample had an average of 3.78 g/100 gDW ($p \leq 0.05$). Particularly during Covid-19 infections, glycine is an excellent superfood supplement. Evans *et al.*, (1951) reported that glycine has potential synergistic effects on food processing. In 1951, free amino acids were combined with free carboxyl groups of histidine, lysine, and arginine, as well as free imidazolyl groups, to produce enzymatic cleavage resistance via peptide-type linkages, leading to resistance to enzyme cleavage. The blended technology is the only method used to achieve this goal.

Table 4
Reducing sugar content of the optimal 3 in1 formula comprising *A. seyal* and *A. senegal* gum (PMC and PTC) powder and A. digitata pulp (ADLP) powder at g/100 g DW unit.

Reducing Sugar	PMC&PTC (Blended 2in1) Mean ± S.D.	ADLPs	Optimum formula (Blended 3in1)
Arabinose	(g/100gDW) 48.23 ± 0.58^{b}	(g/100gDW) 2.27 ± 0.28^{k}	(g/100gDW) 49.97 ± 0.58^{a}
Galactose	36.96 ± 1.3^{c}	0.95 ± 0.12^{l}	37.16 ± 0.59^{c}
Rhaminose	16.39±0.59i	0.95 ± 0.15^{l}	17.16 ± 0.60^{h}
Glucouronic acid	19.19 ± 1.30^{g}	27.27 ± 0.56^{e}	32.237 ± 1.50^{d}
Fructose	0.093 ± 0.002^{m}	3.57 ± 0.23^{j}	3.63±0.23j
Glucose	N.D (<0.001)	3.70 ± 0.17^{j}	3.76 ± 0.11^{j}
Sucrose	N.D (<0.001)	22.16 ± 0.59^{f}	22.16 ± 0.60^{f}
Maltose	N.D (<0.001)	N.D (<0.001)	N.D (<0.001)
Lactose	N.D (<0.001)	N.D (<0.001)	N.D (<0.001)

Note: * Mean value ± SD in raw, followed by different superscript letters indicates a significant difference ($p \leq 0.05$) between rows. **PMC**, A. senegal gum (commercial); **PTC**, *A. seyal* gum (commercial); **ADLPs**, A. digitata pulp powder; **EAA**: Essential Amino Acids; **NEAA**: Non-essential Amino Acids.

3.5. Evaluation of reducing sugar in the optimum formula

Evaluation of the reducing sugar content in the optimum formula revealed intriguing insights. Reducing sugars, which are known for their capacity to reduce other substances and form sugar-acid mixtures, displayed notable variation among blended samples (Du *et al.*, 2023; Li *et al.*, 2023b; Vats *et al.*, 2024; Wang *et al.*, 2023a). In particular, the blended 3 in1 sample exhibited the highest concentration of arabinose, a key component. Arabinose content was 48.23 g/100 g DW in the 1 in1 ADLP sample and 49.97g/100 gDW in the 3 in1 sample. The blended 2 in1 sample had a significantly lower arabinose value (2.27 g/100 g DW) than the blended 3 in1 sample. These findings align with previous studies; Lopez *et al.*, (2015) reported *A. seyal* gum and *A. senegal* gum (blended 2in1) gum arabinose values of 30.3 and 47.60g/100gDW, respectively.

Similarly, Menzies *et al.* (1996b) reported arabinose concentrations of 24–29 g per 100 g DW for *A. seyal* gum, and 41–45 g per 100 g DW for *A. senegal* gum. g/100 g DW in a blended 1 in1 ADLP sample (Alba *et al.*, 2020). Schwarz *et al.* found that the arabinose residues at 2.3 M inhibit Covid-19channels effectively (2014). The amalgamation of *A. senegal, A. seyal*, and ADLP resulted in an increased arabinose concentration in the formulation, providing valuable insights into the possibility of arabinose preventing Covid-19 infection.

3.5.1. Galactose content

The evaluation of the galactose content in the blended samples yielded exciting findings. Galactose, a monosaccharide sugar with a lactose component and milder sweetness than glucose, exhibits varying concentrations across formulations (Budin, 2024; Jelen, 2022). Specifically, the blended 2 in1 and 3 in1 samples displayed galactose content of 36.96g/100 gDW and 37.17g/100 gDW, respectively, whereas the blended 2 in1 and 3 in1 samples displayed galactose content of 36.96g/100 g DW and 37.17g/100 g DW, respectively. In a previous study, Lopez *et al.* found galactose levels of 35.8 g/100 g DW for *A. senegal* and *A. seyal* gum (blended 2 in1) (2015), while Menzies *et al.* found 36 g/100 g DW and 42 g/100 g DW (1996b). In the blended 1 in 1 ADLP sample, Alba *et al.* also found galactose values of 0.90g/100 gDW (2020). Notably, significant differences were observed ($p \leq 0.05$), highlighting subtle variations in the galactose content among the samples. Interestingly, the galactose and rhamnose contents in the blended 1in1 ADLP sample were similar, with an average value of 0.95g/100gDW. However, these differences were statistically significant ($P \leq 0.05$). The 3 in1 blend showed the highest galactose content, highlighting the significant differences in sugar composition among the samples.

3.5.2. Glucuronic acid

The evaluation of the galactose content in the blended samples yielded interesting findings. Galactose, a monosaccharide sugar with a lactose component and milder sweetness than glucose, exhibits varying concentrations across formulations (Budin, 2024; Otter *et al.*, 2022; Poka *et al.*, 2023). Specifically, the blended 2 in1 and 3 in1 samples displayed galactose content of 36.96g/100 gDW and 37.17g/100 gDW, respectively. Previous research by Lopez *et al.* reported galactose levels of 35.8 to 36.9g/100 gDW for *A. senegal and A. seyal gum* (blended 2 in1)(2015), whereas Menzies *et al.* showed concentrations of 36 g/100 g DW and 42 g/100 g DW (1996a). A similar mean galactose concentration in a blended 1 in 1 ADLP sample was reported by Alba *et al.* (2020). Notably, significant differences were found ($p \leq 0.05$), highlighting subtle variations in galactose content between the samples. Interestingly, 1in1 ADLP samples containing more galactose and rhamnose showed similarity, with an average value of 0.95 g/100 g DW, although the differences were still statistically significant ($p \leq 0.05$). Overall, the study showed significant variations in galactose content, with the 3 in1 blend having the highest concentration, which is consistent with previous research.

3.5.3. Sucrose content

Sucrose, commonly known as table sugar, is formed by a combination of glucose and fructose. Sucrose levels were acidic in mixed 3in1 samples. Table 4 shows that the average sucrose content in the combined 1in1 ADLP and 3in1 sample was 22.17 g /100gDW. Despite a slight difference in sucrose content between the 2 samples, the mean sucrose concentration in the combined 1in1 ADLP sample and the combined 3in1 sample was significantly ($p \leq 0.05$) higher than that in the combined 2in1 sample, whose sucrose concentration was less than 0.001 g/100gDW. The levels of reducing sugars exhibited significant variations among the 3 blended samples sourced from the same location. The lowest rhamnose value observed was 0.95g/100 gDW, while the highest value was 16.39g/100 g DW for the combined 1 in1 ADLP and 3 in1 samples, respectively.

In Table 4, the fructose and glucose levels in the combined 1 in1 ADLP and 3 in1 samples typically ranged from 3.57 to 3.77g/100 gDW, with an average of 3.67g/100 gDW. However, ANOVA did not reveal any significant differences ($p \leq 0.05$) between the blended samples and those without ADLP. In the *A. senegal* and *A. seyal* samples, fructose and glucose contents were nearly negligible, ranging from 0.00 to 0.093 g/100 g DW, whereas the blended 3 in1 sample had a content of approximately 3.63 g/100 gDW. There were no noteworthy variations in the fructose and glucose levels among the 3 selected samples ($p \geq 0.05$). Notably, maltose and lactose were not detected in any sample.

3.6. Limitations and Future Research Direction

This study provides a detailed analysis of a novel 3 in1 blend aimed at enhancing the human innate immune system (HIIs), particularly in COVID-19 patients with Metabolic Syndrome (MeT-S). However, like any scientific study, it has limitations and areas for future research, as follows:

Limitations:

1. **Sample Size and Diversity**: The study might have limitations regarding the sample size and diversity of the population studied. Expanding the sample size and including a more diverse group of participants can help generalize the findings.
2. **Short-term Study Duration**: The effects of the 3 in1 blend on HIIs were observed over a short period. Long-term studies are necessary to understand the sustained impact of this blend on immune function and metabolic health.
3. **Control Groups and Blinding**: The study design details regarding the control groups and whether the study was blinded are not specified. Future studies should include these aspects to minimize bias and enhance the reliability of the results.
4. **Mechanistic Insights**: While study provides data on the nutritional content and potential health benefits of the blend, mechanistic insights into how these effects are achieved at the molecular level are limited. This is discussed in part 2.
5. **Clinical Outcomes**: The study primarily focused on biochemical markers and immune responses. The clinical outcomes related to COVID-19 severity, recovery rates, and long-term health impacts of the blend have not been thoroughly explored.

Future Research Directions

1. **Longitudinal Studies**: Conducting long-term longitudinal studies to monitor the effects of the 3 in1 blend over extended periods can provide insights into its long-term safety and efficacy.
2. **Expanded Clinical Trials**: Implementing larger, multicenter clinical trials with diverse populations can help validate the findings and support the use of the formulation in broader demographic groups.
3. **Comparative Studies**: Comparing the 3 in1 blend with other nutritional supplements or therapeutic interventions for COVID-19

and MeT-S can help position the blend within the current treatment landscape.
4. **Mechanism of Action Studies**: Investigating the molecular mechanisms through which the blend exerts its effects could lead to a deeper understanding and optimization of the formulation.
5. **Economic and Accessibility Analysis**: Assessing the economic impact and accessibility of producing and distributing the 3 in1 blend, especially in low-resource settings, can help in planning its practical deployment.
6. **Integration with Other Therapies**: Exploring the synergistic effects of the 3in1 blend with other therapies, such as pharmacological treatments for COVID-19 and lifestyle modifications for MeT-S, could provide a holistic approach to management.

Finally, these suggestions for future research and acknowledgment of the limitations are crucial for advancing the scientific understanding and practical application of the 3 in1 blend in boosting the human immune system against COVID-19 and related metabolic disorders.

4. Conclusion

This study combined *A. senegal* and *A. seyal* with ADLP as a potentially promising therapeutic approach for Covid-19, particularly in patients with MeT-S. In addition to essential molecular structures and micronutrients, the optimized 3in1 blend formula also contains carbohydrates, functional proteins, essential minerals (K, Ca, Mg, P, and Na), EAAs (such as hydroxyproline and arginine), sugars, prebiotics, and trace elements (such as Zn, Fe, Cu, and Se). Throughout history, these nutrients have proven pivotal in preventing Health-Related Infections (HIIs) and lowering susceptibility to asymptomatic infections. The role of Zn and Se in bolstering antiviral defenses and supporting antiviral mechanisms underlies their importance. Individuals infected with the virus should receive adequate supplementation of these essential nutrients. A comprehensive analysis of the findings of this study revealed significant economic benefits. HIIs can be enhanced by eating a variety of plant-based and animal-based foods, according to contemporary healthy eating guidelines. The outcomes of this study suggest that the innovative 3 in1 blend comprising *A. seyal* and *A. senegal*, along with ADLP, has the potential to be regarded as a natural source of superfood, offering substantial support to HIIs and contributing significantly to the battle against the Covid-19 pandemic.

Availability of data and materials

The datasets used in this study are provided upon request by the authors.

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Declaration

The authors reviewed and edited the manuscript as needed, taking full responsibility for its content. Professional proofreading services were employed to correct grammatical errors and sentence structures. In the following step, Turnitin was used to conduct a similarity check of the manuscript, which resulted in a similarity score of 0%, with 0% AI similarities. Furthermore, we have included all related data as supplementary files and the similarity report, which is well within acceptable publication standards.

CRediT authorship contribution statement

Ahmed A.M. Elnour: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Nour Hamid Abdurahman:** Visualization, Validation, Supervision, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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