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(54) Title: A NOVEL NUTRACEUTICAL FORMULATION FOR POLYCYSTIC OVARY SYNDROME (PCOS)

(57) Abstract: The invention is a nutraceutical food supplement for treatment of young women in post-puberty age suffering from polycystic ovary syndrome with symptoms like irregular menstruation cycles, insulin resistant diabetes, infertility, hair loss, acne and weight gain. While limited success has been achieved in treating infertility with inositol isomers in combination with folic acid and vitamins, the nutrient supplement described in the present invention Protisol has proved significantly enhanced effectiveness in controlling the varied symptoms of PCOS. It is a formulation containing myo-inositol and its d-chiro isomer with specific plant proteins mostly from peas and rice, a carbohydrate (inulin) and other plant fibres; a defined proportions of vitamins (A, B₁₀₆, B₁₂ and C); several minerals like Ca, Cr, Fe, K, Mg, Mn, Na and Zn and essential amino acids like L-Glutamine, L-Lysine, and L-Taurine. In a pilot study a dose of 20 gms twice daily has resulted in significantly enhanced effectiveness than that achieved by conventional treatment modality. The synergistic effect of the plant proteins is ascribed to the proteins acting as effective transport carriers of inositol isomers.



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5 **TITLE: A NOVEL NUTRACEUTICAL FORMULATION FOR
POLYCYSTIC OVARY SYNDROME (PCOS)**

TECHNICAL FIELD OF INVENTION:

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[0001] NUTRIANT SUPPLIMENT

[A nutrient food supplement for treatment of insulin resistant Polycystic Ovary Syndrome (PCOS)]

15 **BACKGROUND ART:**

INTRODUCTION

20 **[0002]** Polycystic Ovary Syndrome (PCOS) is a disease defined by a collection of signs and symptoms frequently seen in women during their post-puberty age. The major symptoms vary from person to person. The most common symptoms of PCOS are : (i) irregular or missing menstrual cycle; (ii) infertility; (iii) excess bleedings; (iv) unwanted body or facial hair growth; (v) thinning of hair on the scalp; (vi) weight gain around the waist; (vii) skin problems including skin tags, skin darkening and (viii) appearance of acne. If there be two or more of these symptoms the person needs a thorough medical check-up to determine the treatment modality. Although the root cause of PCOS being still unknown, the various contributory factors are (i) stress, (ii) dietary habits, (iii) genetic disposition, (iv) pollution, (v) excess insulin production and (vi) low grade inflammation. As the symptoms of PCOS are multi-faceted, the presently practiced treatment is mostly symptomatic like use of fertility and birth

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control pills to regulate menstruation, medications for insulin sensitization with metformin and/or with inositol isomers (myo- and d-Chiro) and topical anti-hair growth creams and other such medications. Emphasis is laid also on life style modifications and specialized restricted dietary regimens for weight control of PCOS patients.

[0003] Polycystic Ovary Syndrome (PCOS) is a hormonal disorder normally occurring in post-puberty women of reproductive age group. In such cases, when there occurs a hormonal imbalance and the levels of male hormone androgen becomes high in women it gets stored in small globules inside the ovary which finally results in a cystic formation. Hence it is named as Polycystic Ovary Syndrome (PCOS) or Disorder (PCOD).⁽¹⁾

[0004] The excess production of male hormones in women leads to growth of unwanted hair on face or other parts of body that is normally not seen in women. It also causes thinning or loss of hair on the scalp, causes acne and leads to hypertension and insulin resistant diabetes. The unbalance due to lower level in female hormone (progesterone) causes irregularities in the menstruation cycle; reduces chances of pregnancy and leads to total infertility. Such women also tend to gain weight around the waist

PRIOR ART

[0005] Unfortunately, no single root cause of PCOS is identified till date and only the symptomatic treatments are presently prescribed. For instance, metformin and a combination of inositol isomers have often been recommended for treatment of infertility, hair growth inhibiting topical creams are advised and hair transplant for overcoming hair thinning on scalp are recommended and are being tried. Life-style

changes and strict dietary regimens are suggested for weight gain and diabetes.

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SUMMARY

The invention Protisol is a well-defined formulation containing fixed amounts of energy supplying leguminous and non-leguminous plant proteins derived from peas and rice that are wholesome and muscle energy suppliers and are also free from contaminants like saturated fatty acids, cholesterols and residual hormones normally associated with animal proteins. The plant proteins derived from soya and pea-nuts that may contain allergens are specifically excepted. The Protisol also contains carbohydrates and plant fibres and a well defined proportion of vitamins (A, B_{1 to 6}, B₁₂ and C); vitamin like substances such as biotin, myo-inositol and its isomer d-chiro inositol; folic acid, a host of several minerals (Ca, Cr, Fe, K, Mg, Mn, Na and Zn) in their various edible chemical compounds and essential amino acids like L-Glutamine, L-Lysine, and L-Taurine.

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In a pilot study with a dose of 20 gms of Protisol used in a defined protocol for 3 months, the symptoms of PCOS were successfully treated in over 90 percent of patients in a cohort of about 1000 young women from the cities of India like Mumbai, Pune, Delhi and Ahmadabad. In an infertility clinic trial spread over one year, nine successful pregnancies were noted out of the 12 semi-urban women undergoing treatment with Protisol.

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DISCLOSURE OF THE INVENTION

[0006] The limitations in the scientific knowledge on the root cause of PCOS and the multiplicity of its probable causes leading to multiple

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symptoms and absence of any single comprehensive treatment for all its symptoms and only individual symptomatic relief being recommended, necessitated research that has led to the development of the present
95 product invention tentatively named PROTISOL which is a nutraceutical formulation that provides complete and comprehensive treatment of PCOS. It essentially is a nutritional supplement to be taken twice daily with ease and taste that has proved to be a single highly efficient remedy for treatment of all the symptoms of PCOS.

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[0007] Briefly, it contains inositol isomers with several vitamins and vitamin like substances, a defined proportion of host of minerals and essential amino acids and other several such plant materials like leguminous and cereal proteins derived basically from peas and rice. The
105 proteins so selected by work as carriers and/or facilitators and act in synergism with inositol isomers in the enhanced effective treatment of PCOS particularly for the insulin resistant women in their post-puberty reproductive age. It is this aforesaid synergism between the ingredients that is being claimed as the Novelty of the product.

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[0008] The invention Protisol is a well-defined formulation containing fixed amounts of energy supplying leguminous and non-leguminous plant proteins derived from peas and rice that are wholesome and impart adequate muscle energy to patients and are also free from
115 weight gaining contaminants like saturated fatty acids, cholesterol and residual hormones normally associated with animal proteins. The plant proteins derived from soya and pea-nuts that may contain allergens are specifically excepted. The Protisol also contains carbohydrates and plant fibres and a well defined proportion of vitamins (A, B_{1 to 6}, B₁₂ and C);
120 vitamin like substances such as biotin, myo-inositol and its isomer d-

chiro inositol; folic acid, a host of several minerals (Ca, Cr, Fe, K, Mg, Mn, Na and Zn) in their various edible chemical forms and the essential amino acids like L-Glutamine, L-Lysine, and L-Taurine. The composition of a representative 20 gm Protisol dose is given in the Table

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[0009] In a pilot study with a dose of 20 gms of Protisol used twice daily, the symptoms of PCOS were successfully treated in over 90 percent of patients in a cohort of about 1000 young women from the cities of India like Mumbai, Pune, Delhi and Ahmadabad. In an infertility clinic trial spread over one year, nine successful pregnancies were noted out of the 12 women from a semi-urban city in India namely Panvel near Mumbai undergoing treatment with Protisol.

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INDUSTRIAL APPLICABILITY

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[0010] In an exhaustive randomized Clinical trial (Phase -4) with 46 young women suffering from PCOS and hyper-insulemia the beneficial effect of drugs like m-inositol, d-chiro inositol plus foilic acid has been studied.⁽²⁾

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[0011] The present product invention lies in the fact that Protisol is not any drug but a food supplement containing clinically permissible and regularly used pharmaceuticals in proportions as these exist in a normal women or are normally recommended for use by Indian Council of Medical Research (ICMR). The invention product mainly contains plant based leguminous and cereal proteins derived from Pea and rice that are rich in absorbable iron and contains nine essential amino acids but none of the food allergens that exist in proteins of peanut, cow's milk, eggs, soya, fish and wheat. It may contain carbohydrate inulin and other plant fibres. The invention Protisol contains not only myo- and d-Chiro-inositol

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150 + Folic acid but also 25 vitamins and a host of salts/compounds of
minerals naturally present and required for healthy human body. ⁽³⁾

[0012] In particular the pea protein powder (concentrate and isolate)
which is the second major constituent (>40%) of the present invention
155 product is a facilitator to work as a transporter/ carrier for the myo-
inositol and its isomer d-chiro inositol that renders a synergistic influence
on their overall ability to treat of PCOS in women without causing any
adverse effects.

160 EXPERIMENTAL RESULTS

[0013] In a preliminary trial of large cohort comprising of about
1000 women in their post-puberty age with various symptoms of PCOS
coming from urban background of Mumbai, Pune, New Delhi and
165 Ahmadabad were treated with Protisol. The results revealed that over 90
percent of them reported partial and/or complete cure. No adverse effects
have been reported to the treating physicians.

[0014] A small three month therapeutic clinical trial with Protisol
170 was conducted on 12 infertile women in child bearing age from a small
semi-urban town of Panvel, near Mumbai in India with the following
protocol.

(i) in the 1st month a 20gm dosage was given twice daily soon after
175 the breakfast (Or replacing the breakfast altogether in the obese
women) and the second dose given before Dinner

(ii) during 2nd & 3rd Month if the symptoms are under control a
dose of 20 gm was recommended once a Day after breakfast (Or
180 totally replacing the breakfast for the obese women)

[0015] The results showed that 9 women of (75%) the group receiving the treatment had successfully conceived within one year without any untoward complications relating to the treatment.

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[0016] Physician's further clinical Feedback in general:-

(i) Most of the PCOS symptoms were controlled after 1 month of treatment which could not be achieved with 6 months of treatment with m-inositol alone.

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(ii) PCOS remained under control in the above mentioned three months schedule of treatment without any relapse on follow-up for 1 year.

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The invention nutraceutical formulation PROTISOL is therefore patentable.

[0017] CITATIONS

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1. <https://www.webmd.com/women/what-is-pcos>
2. <https://clinicaltrials.gov/ct2/show/NCT01626443>
3. <https://www.healthline.com/nutrition/pea-protein-powder#nutritional-benefits>

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TABLE**APPROXIMATE COMPOSITION OF 20 GM PROTISOL PORTION
Blend- Pea and rice protein (<43.5%) and dietary plant fibres (<65%)**

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Material	Amount	% RDA
Myo-inositol	2 gm	NA
D-Chiro inositol	0.05gm	NA
Inulin	1.3 gm	NA
Vit. C	40 mg	100
Calcium Carbonate	40 mg	2.6
Magnesium Sulfate	40 mg	2.37
Zinc Sulfate	30 mg	100
Vit B ₅	15 mg	
Sod. Chloride	10 mg	0.18
Potassium Chloride	10 mg	0.10
Vit.B ₃	2.2 mg	12.2
Ferrous Fumerate	2 mg	3.88
Vit. B ₆	2mg	100
Vit B ₂	1.6 mg	100
Vit.B ₁	1.4 mg	100
Manganese Sulfate	0.6 mg	4.36
Folic Acid	0.2 mg	100
Vit.A (acetate)	0.02 mg	3.33
Sod. Selenite	40 mg	45.56
Biotin	30 mg	**
Chromium Picolinate	2 mcg	0.12
Potassium Iodie	2 mcg	1.01
Vit. B ₁₂	1 mcg	100
L-Glutamine	0.85 mcg	NA
L-Taurine	0.71 mcg	NA
L-Lysine	0.56 mcg	NA
Vit.D	400 I.U.	NA

Note ; RDA - Recommended Daily Allowances as per the guidelines of Indian Council of Medical Research (ICMR)

CLAIMS

We claim:

- 5 1. A nutraceutical Food Supplement Formulation Product named Protisol.
- 2 The Product in Claim No.1 contains a powdered mixture of 65% or less
of plant fibres with maximum 43.5% of blends of leguminous and cereal
10 proteins like concentrates and isolates of peas and rice,
3. The Product in Claim No.1 also contains myo-inositol upto 10 percent
with its isomer d-chiro inositol at concentrations in ratio of 40:1.
- 15 4. The Product in Claim No.1 may contain vitamins (A, B₁ to B₆, B₁₂, Vit
C and Vit D) and vitamin like substances such as biotin and folic acid in
quantities as found in or recommended by ICMR for healthy normal
women in post puberty age,
- 20 5. The Product Claim No.1 may also contain several minerals (Ca, Cr, Fe,
K, Mg, Mn, Na and Zn) in their various chemical forms like chlorides,
sulfates, carbonates etc. in quantities normally found in or as
recommended by ICMR for healthy women in their post-puberty age.
- 25 6. The Product Claim No.1 may also contain essential amino acids like L-
Glutamine, L-Lysine, and L-Taurine in quantities as found in healthy
normal women in their post-puberty age or as recommended by ICMR for
them,
- 30 7. The Product in Claim No.1 when orally given twice or thrice at daily
doses of about 20 gms for more than one month to treat women with

PCOS is more effective than those treated at with presently followed protocol using myo-inositol with d-chiro inositol and folic acid or a combination thereof

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2020/000019

A. CLASSIFICATION OF SUBJECT MATTER A23L33/00 Version=2020.01		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) A23L		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Database: TotalPatent One, IPO Internal Database Keywords: PCOS, Plant fiber, protein, vitamin, mineral		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Kazemi, M., et.al., "A Comparison of a Pulse-Based Diet and the Therapeutic Lifestyle Changes Diet in Combination with Exercise and Health Counselling on the Cardio-Metabolic Risk Profile in Women with Polycystic Ovary Syndrome: A Randomized Controlled Trial." <i>Nutrients</i> , 2018, 10(10), 1387. doi:10.3390/nu10101387 *Refer to the whole document*	1-7
Y	Turner-McGrievy, G. M., et.al., "Low glycemic index vegan or low-calorie weightloss diets for women with polycystic ovary syndrome: a randomized controlled feasibility study." <i>Nutrition Research</i> , 2014, 34(6), 552-558. doi:10.1016/j.nutres.2014.04.011 *Refer to the whole document*	1-7
Y	Günalan, E., et.al., "The Effect of Nutrient Supplementation in Management of Polycystic Ovary Syndrome Associated Metabolic Dysfunctions: A Critical Review." <i>J Turk Ger Gynecol Assoc.</i> 2018 Dec; 19(4): 220-232.,	1-7
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "D" document cited by the applicant in the international application "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 30-12-2020		Date of mailing of the international search report 30-12-2020
Name and mailing address of the ISA/ Indian Patent Office Plot No.32, Sector 14, Dwarka, New Delhi-110075 Facsimile No.		Authorized officer Trishala Verma Telephone No. +91-1125300200

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PCT/IN2020/000019

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	doi:10.4274/jtgga.2018.00770 *Refer to the whole document*	
Y	----- Faghfoori, Z., et.al., "Nutritional management in women with polycystic ovary syndrome: A review study." Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2017, 11, S429-S432. doi:10.1016/j.dsx.2017.03.030 *Refer to the whole document*	1-7
Y	----- Hariprasath, G. et.al., "Taurine Supplementation Improves Insulin Sensitivity and Lipid Profile in PCOS Women" International Journal of Scientific Research, Volume-7, Issue-1, January-2018, ISSN No 2277 - 8179 *Refer to the abstract*	1-7