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RESEARCH ARTICLE

Asparagus racemosus – A potential PCOD healer through the management of hyperglycaemia and hyperandrogenism, An *In vitro* and *in silico* approach

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ABSTRACT:
Polycystic Ovarian Syndrome is a heterogenous disorder characterized by hyperandrogenism, chronic anovulation and hyperglycaemia. An attempt is made in the present study to reduce the complications of PCOS especially hyperglycaemia and hyperandrogenism through the ethanolic root extracts of *Asparagus racemosus* by performing *in vitro* and *in silico* experiments. *In vitro* experiments such as inhibitory activity of α amylase and glucose adsorption, inhibition of glucose diffusion and glucose uptake by yeast cells were performed concentrating the enteric system to reduce the glucose entry into the blood circulation to manage the hyperglycaemia. *In silico* methods were performed using patch dock to screen the suitable antagonistic phyto ligand from the plant for the IRS1 and IRS 2 receptors for the negative down regulation of androgen production. The selected plant extract exhibited a concentration dependent glucose maintaining activity in the present investigation which was comparable to the positive drug Acarbose which exerts hypoglycemic activity acting as enteric system. In the patch dock analysis five ligands namely Quercetin, Racemosol, Rutin, Hyperoside and Shatavarin I were selected as best antagonistic ligands for the IRS1 and IRS 2 receptors in terms of their docking score and amino acid interactions. It can be concluded that the ethanolic root extracts of *Asparagus racemosus* can be considered as a potential drug for the management of PCOS through their dual role of reducing hyperglycaemia and hyperandrogenism.

KEYWORDS: PCOD, Hyperglycaemia, Hyperandrogenism, IRS, Antagonistic.

INTRODUCTION:
Polycystic ovary syndrome (PCOS) is a multifaceted endocrine disorder among women in their reproductive period characterized by menstrual disorder, hyperandrogenism, hirsutism, and persistent absence of ovulation with multiple cysts in the ovary[1,2]. It affects nearly 2.2-26% of women in their reproductive age in India[3]. The synergistic pathology of increased androgens and hyperinsulinemia in PCOS aggravates the risk for metabolic syndrome such as Impaired glucose tolerance (IGT), type 2 diabetes mellitus, obesity, dyslipidemia and nonalcoholic fatty liver disease which is mainly due to insulin resistance[4].

It is well established that insulin manifests both hyperinsulinemia and ovarian hyperandrogenism leading to chronic anovulation[5].

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In excess insulin status, along with luteinizing hormone (LH) it has a stimulatory effect on steroidogenesis of granulosa cells by enhancing human chorionic gonadotropin (hCG)-leading to cyst formation in PCOS condition[6]. There are several studies which suggest that the insulin exerts its androgen-stimulating effect through the binding of the insulin receptors[7]. Insulin receptor substrate proteins (IRS-1 and IRS-2) act as receptors for the ligands such as insulin, other tyrosine kinase dependent growth factors and cytokines[8]. Recent studies indicate that polymorphisms in IRS receptors may increase the risk of type-2 diabetes mellitus in PCOS women since insulin mediated actions differ in insulin target tissues.

At present the management of PCOS includes lifestyle modifications in the form of dietary changes which includes reduced carbohydrate and fat intake, exercise for weight reduction and allopathic treatment consisting of anti-androgens, insulin sensitizing drugs and ovulation inducing drugs. But these treatments have side

effects such as irregular menstruation, gastrointestinal disturbances, weight gain, and increased insulin resistance[9]. While developing alternative medication, plant-based drugs are used. Medicinal plants perform complex interventions through synergistic or antagonistic interactions with receptors[10].

Asparagus racemosus (Liliaceae), commonly known as Shatavari, is present in India, Australia, Africa and Asia. It is consumed as a vegetable in many parts of the world. The shoots are edible and mostly used in soups, vegetable dishes and salads. In India, it has been used for the treatment of diarrhea, dysentery, nervous breakdown, rheumatism and microbial infection due to its various medicinal properties[11,12]. Studies revealed that the phytochemical compound of *A. racemosus* constitutes oligosaccharides, flavonoids, steroidal saponins and sulphur – containing amino acids[13]. Studies have been reported for decreased intestinal propulsive movement in the methanolic extract, in castor oil induced diarrhea and fluid accumulation in rats. It has also been reported to decrease gastric emptying[14]. The meaning of *Shatavari* is "women who can have hundred husbands" implicating its potency to treat all women's health issues[15]. With this above scenario we made an attempt to study ameliorative activity of ethanolic root extract of *A. racemosus*, on PCOS associated hyperglycemia and hyper androgonemia through *In vitro* and *in silico* approach.

MATERIALS AND METHODS:

Preparation of crude extract:

The roots of the plant were shade dried, ground into coarse powder and stored in an airtight container. It was subjected to ethanol extraction in the ratio (1:3) by cold maceration method for three days. The extract was filtered, evaporated using a rotary evaporator and refrigerated.

In vitro antidiabetic activity:

The following antidiabetic activities were carried out. α-amylase enzyme inhibiting effect of the plant extract was studied by the method of Jayasri *et al.*[16], inhibitory action of Glucose diffusion was calculated by the method of Gallagher *et al.*[17], glucose uptake by yeast cells was performed by Cirillo[18] method and measurement of glucose adsorption potential by plant extract was studied by the method of Ou *et al.*[19].

In silico anti-hyperandrogenic activity:

It was carried out by molecular docking using patch dock analysis to find a fitting ligand of the plant compound as a competitive inhibitor for the receptor IRS 1 and IRS 2. The 3D structure of the receptors was taken from PDB (Protein data bank). The phytochemical compounds of the plant were known from the GC-MS studies of Hayes *et al.*,[20] Singh and Tiwari,[21] Ahmad and Jain,[22]. Patch dock analysis was done for 14 compounds. The 2D structure of *A. racemosus* phytochemicals were retrieved from PubChem. Corina 3D converter was used to obtain its 3D structure. The score of ligand and receptor interaction was obtained from patch dock server. The best docking score was selected and inhibitory potential of the phytoconstituents of *A. racemosus* was analyzed by interactions with amino acid residues at the active site. It was visualized and confirmed by LIGPLOT.

Statistical analysis:

The values are reported as Mean ± SD (n = 3). the statistical analysis was done using ANOVA followed by Dunnet's "t" test. Values of $p<0.05$ were considered.

RESULTS:

α Amylase inhibitory activity:

Figure 1 shows α amylase enzyme inhibitory activity of *A. racemosus* at different concentrations. From the present study, it was very prominent that the ethanolic extract of *A. racemosus* inhibited α amylase enzyme at a low concentration compared to the control Acarbose. The IC 50 value for the study is 367µg/ml.

Inhibitory activity of Glucose diffusion:

The inhibitory effect of glucose diffusion by the plant extract at different concentrations is shown in Figure 2. The ethanolic extract of *A. racemosus* inhibits the glucose diffusion at all given concentrations and an enhanced activity is observed at higher concentration of 1000 µg/ml. At this concentration the plant extract and the standard drug (Acarbose) showed almost similar inhibition of glucose diffusion.

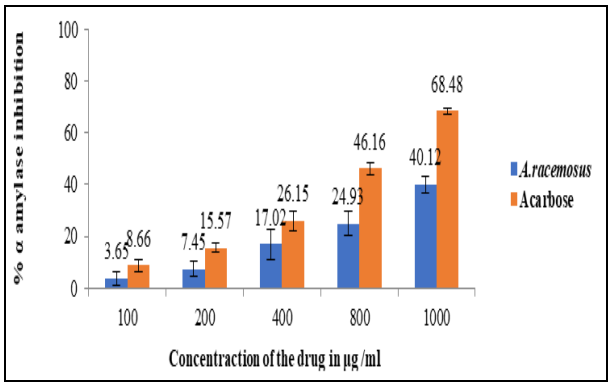


Figure 1: Inhibitory activity at different concentrations of *A. racemosus* and Acarbose on α Amylase enzyme.
Each value represents the mean±SD (n = 3)

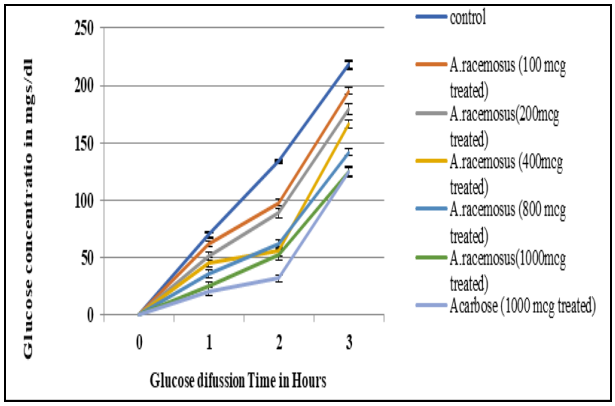


Figure 2: Inhibitory activities at different concentrations of *A.racemosus* and Acarbose on Glucose diffusion.
Each value represents the mean±SD (n = 3)

Measurement of Glucose uptake by yeast cells:

The percentage of glucose uptake by plant extract and the drug can be viewed from Figure 3. There was a concentration dependent increase of glucose uptake by the plant extract treated yeast cells. This shows that the phytochemicals present in the ethanolic extract of *A. racemosus* mimics the action of insulin thereby aids in the entry of glucose molecules inside the yeast cells.

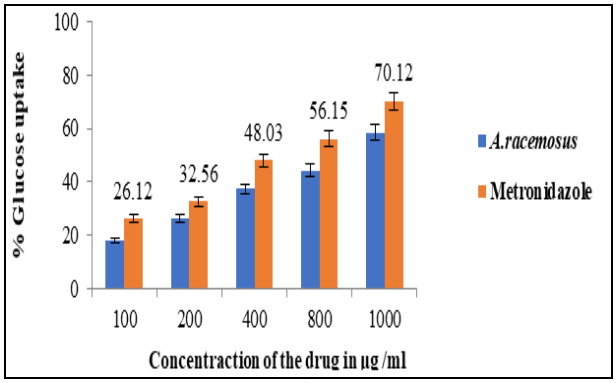


Figure 3: Inhibitory activities of *A.racemosus* and Metronidazole on Glucose uptake by yeast cells.
Each value represents the mean±SD (n = 3)

Measurement of Glucose adsorption potential by plant extract:

Figure 4 shows the glucose adsorption potential of the plant extract. It was observed that the glucose adsorption capacity increases with increase in the glucose concentration. In the present study the plant extracts adsorbed glucose at both low and high concentration effectively. Irrespective of the glucose concentration, the drug was able to combine with glucose and thereby retard the absorption across the intestinal lumen.

In silico anti-diabetic activity:

Molecular docking performed for 14 compounds against the receptor IRS 1 and IRS 2 are tabulated with their corresponding docking scores obtained. (Table 1)

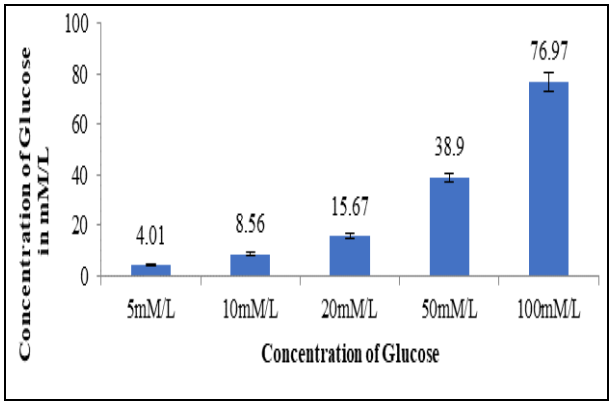


Figure 4: Glucose adsorption capacity of *A. racemosus* extract at different concentration of Glucose.
Each value represents the mean±SD (n = 3)

Table 1 - Docking score values of phytochemicals of *Asparagus racemosus* with IRS 1 and IRS 2

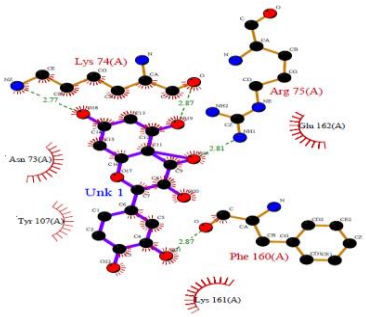
S.No	Compound Name	Binding energy expressed in (kJ mol^{-1})	
		Insulin Substrate Receptor 1(IRS-1)	Insulin Substrate Receptor 2 (IRS-2)
1	Oligospirotinosides	-0.78	-1.02
2	Thiophene	-0.12	-7.07
3	Quercetin 3-O-Glucoronide	-0.32	-0.96
4	Racemosol	-0.01	-0.15
5	Schidigera Saponin	-0.57	-8.02
6	7-O-Beta-D-Glucopyranoside	-0.81	-1.30
7	9,10 Dihydrophenanthrane	--2.58	-6.10
8	Elatin	-0.68	-0.95
9	Hyperoside	-0.61	-0.57
10	Quercetin	-0.08	-0.44
11	Diosgenin	-0.28	-0.67
12	Rutin	-0.31	-0.65
13	Shatavarin 1	-0.46	-0.58
14	Shatavarin 4	-1.33	-0.91

The inhibitory activity of the receptors IRS 1 and IRS 2 with the phytochemicals was performed using Ligplot. From the 14 phytochemicals, Quercetin, Racemosol, Rutin, Hyperoside and Shatavarin I was selected based on their docking score. From Table 2 the interactions between amino acids, the H binding sites and hydrophobic contact sites between the ligands and receptor can be known, and visualized from Figure 5 and 6.

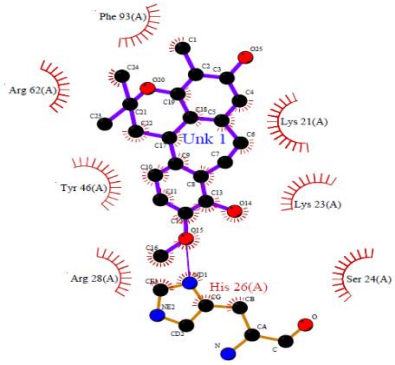
Table 2 - Interaction of IRS 1 and IRS 2 receptor with the phytochemicals of *Asparagus racemosus*

S. No	Compound	Insulin Receptor Substrate 1 (IRS1) receptor amino acid binding site		Insulin Receptor Substrate 2 (IRS2) receptor amino acid binding site	
		H bonding sites	Hydrophobic contact sites	H bonding sites	Hydrophobic contact sites
1	Quercetin	4	63	2	14
		Lys 74 (A), Arg 75 (A), Phe 160 (A)	Asn 73 (A), Lys 74 (A), Arg 75 (A), Tyr 107 (A), Phe 160 (A), Lys 161 (A), Glu 162 (A)	Thr 286 (A), Glu 289 (A)	Asn 282 (A), Thr 286 (A), Glu 289 (A)
2	Racemosol	-	47	-	24
		-	Lys 21 (A), Lys 23(A), Ser 24 (A), His 26 (A), Arg 28 (A), Tyr 46 (A), Arg 62 (A), Phe 93 (A)	-	Lys 203 (A), Pro 204 (A), Lys 205 (A), Phe 254 (A), Gln 273 (A)
3	Rutin	2	50	-	14
		Lys 74 (A), Asn 248 (A)	Lys 74 (A), Arg 75 (A), Ala 76 (A), Lys 81 (A), His 82 (A), Gln 103 (A), Val 244 (A), Gln 247 (A), Asn 248 (A), Glu 251 (A)	-	Lys 203 (A), Ser 251 (A), Phe 254 (A), Trp 271 (A)
4	Hyperoside	8	56	3	66
		Lys 15 (A), Ser 105 (A), Gln 112 (A), Arg 116 (A)	Arg 14 (A), Lys 15 (A), Ser 105 (A), Gln 108 (A), Gln 112 (A), Arg 116 (A)	Gln 199 (A), Asn 201 (A), Asp275 (A)	Gln 199 (A), Val 200 (A), Asn 201 (A), Gln 273 (A), Ala 274 (A), Asp 275 (A)
5.	Shatavarin I	1	72	-	51
		Arg 213 (A)	Gly 172 (A), Thr 176 (A), Arg 212 (A), Arg 213 (A), Phe 222 (A), Glu 224 (A), Pro 233 (A), Gly 234 (A), Glu 235 (A), Trp 237 (A)	-	Lys 205 (A), His 250 (A), Ser 251 (A), Glu 269 (A), Trp 271 (A), Gln 281 (A)

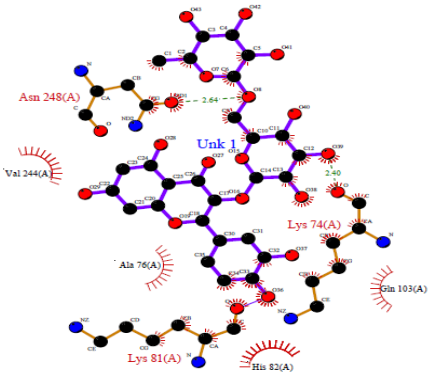
The ligands Quercetin, Racemosol, Rutin, Hyperoside and Shatavarin I had hydrophobic interactions between its amino acids, thus acting as an antagonist ligand for the receptor (IRS 1 and IRS 2). It also acts as a competitive inhibitor thereby exerting the anti-hyper androgenic effect.



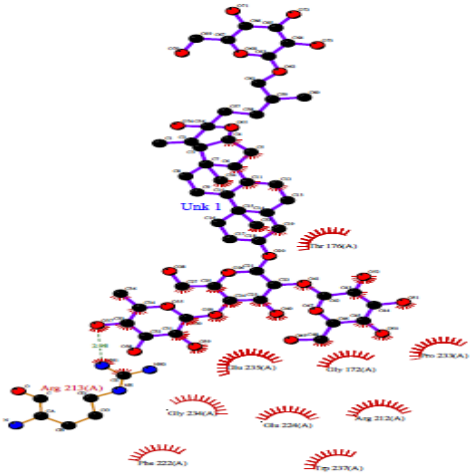
(A) Quercetin



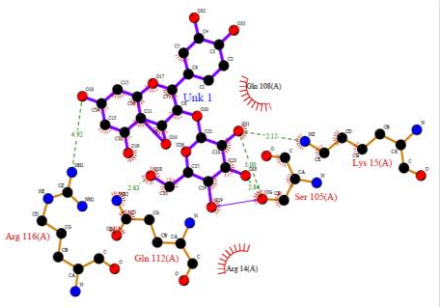
(B) RACEMOSOL



(C) Rutin

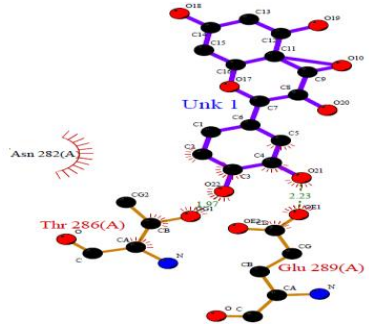


(D) Shatavarin I

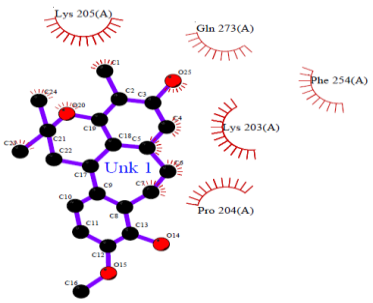


(E) Hyperoside:

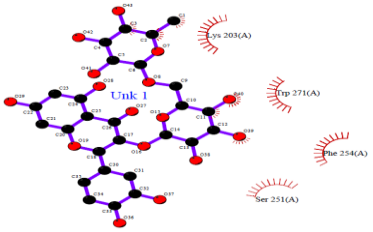
Figure 5: IRS 1 receptor binding with the phytochemicals of *Asparagus racemosus*



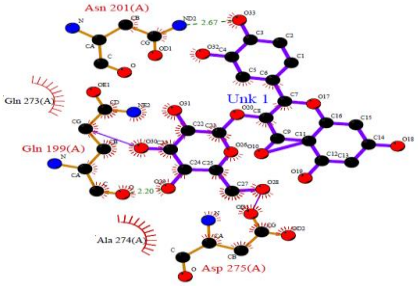
(A) Quercetin



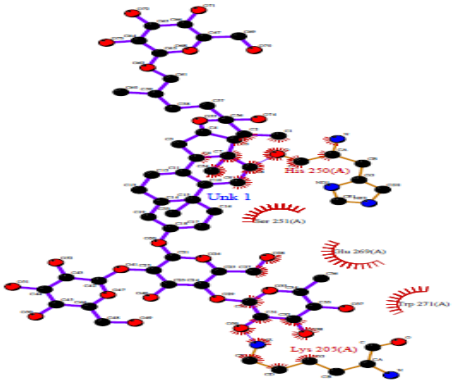
(B) Racemosol



(C) Rutin



(D) Hyperoside



(E) Shatavarin I

Figure 6: IRS 2 receptor binding with the phytochemicals of *Asparagus racemosus*

DISCUSSION:

All over the world, the occurrence of diabetes mellitus is alarmingly increasing. PCOS also contributes significantly to this increased risk of early age type 2 diabetes mellitus (DM) especially in the women population due to peripheral insulin resistance[23.] Insulin controls a wide variety of biological processes including several aspects of metabolism and growth. As a metabolic regulator, it controls carbohydrate, protein as well as lipid metabolism in terms of uptake of glucose and their utilization, protein synthesis, gene transcription and lipogenesis in the specific target tissues. It also acts as a mitogenic regulator in ovaries and controls the steroidogenesis and ovulation along with the insulin-like growth factor termed as insulin/insulin-like growth factor (IGF)-signaling system. Insulin performs these activities through their binding to cell surface receptors called Insulin-receptor substrates IRS-1 and IRS-2. These receptors belong to the class of tyrosine kinase family and they accept insulin, insulin-like growth factor I (IGF-I), epidermal growth factor, fibroblast growth factor and several cytokines as their ligands[24]. At molecular level the binding of the ligand to IRS receptors activates two different downstream signaling pathways namely phosphatidylinositol-3 kinase (PI3K) pathway which regulates the cellular metabolism and the mitogen-activated protein kinase (MAPK) pathway which regulates the cell growth[25].

Several studies have shown a close association between the defective insulin signaling and the pathophysiology of polycystic ovary syndrome (PCOS). These include hyperandrogenemia, (increased androgen production by ovaries) anovulation, hyperinsulinemia and insulin resistance[26]. Moreover, insulin resistance is considered a restricted event, in the sense it will affect only the PI3K pathway, so that the metabolic response to insulin action is impaired. The enhanced activity of MAPK pathway, which is specific to insulin target tissues of the ovary, will not get affected[27]. Moreover Welsh *et al.*,[28] have

also reported that changes in IRS occur as a result of hyperglycaemia, which becomes an etiology of diabetic complications. With this above implication it is clearly evident that PCOS women have metabolic complications including high blood glucose level due to insulin resistance as well as hyperandrogenemia because of the defective insulin signaling. In this context, we made an attempt to investigate the hypoglycemic activity of *A. racemosus*, especially acting on the enteric system to slow down the release of glucose into the circulation for the management of hyperglycemia due to PCOS. Also, we performed *in silico* docking analysis with the phyto molecules of *A. racemosus* to identify a suitable antagonistic ligand for the IRS1 and IRS 2 receptors to suspend the down streaming reactions leading to the complications of PCOS.

There are numerous natural sources which are being investigated for anti-diabetic activity and also for amylase inhibitory activity, a key enzyme in carbohydrate metabolism[29]. In the present investigation, ethanolic extract of *A. racemosus* inhibited α amylase enzyme considerably. According to Vadivelan *et al.*,[30] the total flavonoids and triterpenoids present in the plant extract have the potential to inhibit the digestion of carbohydrates by inhibiting α amylase enzyme and release of glucose. Moreover, studies performed by Hannan *et al.*,[31] in aqueous and butanol extract of *A. racemosus*, indicated low glucose, as well as insulin release pattern could control the hyperglycemic condition. These inhibitory activities are helpful in ameliorating PCOS condition and its associated pathophysiology.

In increasing the blood glucose level, glucose diffusion from the enteric system plays a predominant role. There are plant extracts which slow down the glucose diffusion across the mucosal membrane of the intestine and act as hypoglycemic agents[32]. In the present investigation, ethanolic extracts of *A. racemosus* influences the glucose diffusion and contributed considerably for the hypoglycemic activity. Abdel-Wahab *et al.*,[33] has studied the hypoglycemic effect of *A. racemosus* root extract in the diabetic rats and indicated the inhibition of glucose absorption as one of the tentative mechanisms for the glucose lowering effect. It may be expected that the decrease in the glucose diffusion may be due to the adsorption of the glucose by the phyto molecules which subsequently delay its release in the gastrointestinal tract thereby influencing the diffusion. Irrespective of the glucose concentration, the drug was able to adsorb the glucose and thereby retard the absorption across the intestinal lumen. Studies show the transport of sugars and glycosides across the yeast cell is mediated by stereo specific membrane carriers[34]. Already Hannan *et al.*,[31] have shown that ethanol, chloroform, and hexane root extracts of *A. racemosus* have insulinotropic activity in the sense that the phyto molecules present in the extract mimics the action of insulin thereby helping in the glucose uptake in the cells as evidenced by the yeast cells.

In various cellular substrates, insulin exerts the effects through insulin receptors, particularly IRS proteins intervene the responses of insulin through phosphorylation of tyrosine residue. As already mentioned, the downstream reactions due to this IRS signaling differ in different tissues. Corbould,[35] also in his studies mentioned the same findings, that the expression of IRS protein receptors differs between PCOs affected women and normal women in their adipocytes and muscles. With the clear understanding of hyperinsulinemia in PCOs women, it makes the ovarian theca cells produce androgen in excess leading to hyperandrogenism which is mediated through the binding and signaling of the MAPK pathway. We performed the *in silico* docking analysis to search an antagonist for IRS 1 and IRS 2 receptors, to inhibit the binding of insulin. This will reduce the ovarian hyperandrogenism directly and reduce the other interlinked symptoms like hypersecretion of LH, euglycemic hyperinsulinemia, in association with insulin resistance. We have identified five ligands Quercetin, Racemosol, Rutin, Hyperoside and Shatavarin I which have an antagonistic action against IRS receptor protein. These ligands can act as a competitive inhibitor for the insulin in binding to IRS receptors of theca cells in the ovary thereby inhibiting the mitogenic pathway and excess androgen secretion. Once hyperandrogenism was corrected, the interlinked pathology such as hyperinsulinemia, especially receptor binding action as well as altered LH: FSH ratio was also normalized to prevent the chronic tropic action elicited by these endocrine chemicals.

CONCLUSION:

From the above *in vitro* and *in silico* studies it is concluded that the ethanolic root extract has the ability to treat hyperglycemia and hyperandrogenism, an interrelated complicated pathophysiology occurring in PCOS condition. It may be expected that when hyperglycemia is directly managed through the regulation of enteric glucose, hyperinsulinemia can be controlled indirectly. Moreover, the selected phyto molecules present in the plant extract act as potential antagonistic ligands for the receptor IRS1 and IRS2 which regulates the synthesis of androgens in the ovary. Through their inhibition hyperandrogenism can be reduced. With the dual action of reducing hyperinsulinemia and hyperandrogenism the drug could be prescribed for the management of PCOS cure.

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CONFLICT OF INTEREST:

All the authors enlisted in the manuscript have no conflict of interest.

REFERENCE:

1. Alves MT. de Souza ID. Ferreira CN. Cândido AL. Bizzi MF. Oliveira FR. Reis FM et al Galectin-3 is a Potential Biomarker to Insulin Resistance and Obesity in Women with Polycystic Ovary Syndrome. Gynecological Endocrinology. 2020; 36(9):760-763. DOI: 10.1080/09513590.2020.1739267
2. Pachiappan S. Matheswaran S. Saravanan PP. Muthusamy G. Medicinal Plants for Polycystic Ovary Syndrome: A Review of Phytomedicine Research. International Journal of Herbal Medicine. 2017; 5(2):78-80. DOI:10.31782/IJCRR.2020.122322
3. Anitharajendrababu, Abraham M. Effectiveness of Planned Teaching Programme Regarding Polycystic Ovarian Disease among Adolescent Girls. International Journal of Advanced Nursing Management. 2017; 5(2):143-145. DOI: 10.5958/2454-2652.2017.00030.0
4. Deepthi G. Sankarakumaran P. Jerome A. Kaliarathinam D. Raj NB. US MR. Effect of Aerobic Exercise in Improving the Quality of Life in Polycystic Ovarian Disease. Research Journal of Pharmacy and Technology. 2017; 10(6):1788-1790. DOI: 10.5958/0974-360X.2017.00315.8
5. Dunaif A. Insulin Resistance and the Polycystic Ovary Syndrome: Mechanism and Implications for Pathogenesis. Endocrine Review. 1997; 18(6):774–800. DOI: 10.1210/edrv.18.6.0318
6. Franks S. Gilling-Smith C. Watson H. Willis D. Insulin Action in the Normal and Polycystic Ovary. Endocrinology and Metabolism. Clinics of North America. 1999; 28(2):361–378. DOI: 10.1016/s0889-8529(05)70074-8
7. Nestler JE. Jakubowicz DJ. De Vargas AF. Brik C. Quintero N. Medina F. Insulin Stimulates Testosterone Biosynthesis by Human Thecal Cells from Women with Polycystic Ovary Syndrome by Activating its own Receptor and using Inositol Glycan Mediators as the Signal Transduction System. Journal Clinical Endocrinology Metabolism. 1998; 83(6):2001–2005. DOI: 10.1210/jcem.83.6.4886
8. Myers MG. Sun XJ. White MF. The IRS 1 Signaling System. Trends Biochemical Science. 1994; 19 (7):289–294. DOI: 10.1016/0968-0004(94)90007-8
9. Nowak DA. Snyder DC. Brown AJ. Wahnefried WD. The Effect of Flaxseed Supplementation on Hormonal Levels Associated with Polycystic Ovarian Syndrome: A Case Study. Current Topics Nutraceuticals Research. 2007; 5(4):177-181. PMID: 19789727
10. Williamson E. Synergy and other Interactions in Phytomedicines. Phytomedicine. 2001; 8(5):401–409. DOI: 10.1078/0944-7113-00060
11. Raaman N. Selvarajan S. Balakrishnan D. Balamurugan G. Preliminary Phytochemical Screening, Antimicrobial Activity and Nutritional Analysis of Methanol Extract of Asparagus racemosus (Willd) Roots. Research Journal of Pharmacy and Technology. 2009; 2(4):777-779.
12. Pal RS. Saraswat N. Wal P. Wal A. Pal Y. Maurya D. Pharmacognostic Assessment and Quality Standards of Saraca asoca and Asparagus racemosus. Research Journal of Pharmacy and Technology. 2021; 14(2):949-954. DOI: 10.5958/0974-360X.2021.00169.4
13. Patel LS. Patel RS. Preliminary Phytochemical Analysis and Antimicrobial Activity of In -vitro Condition Asparagus racemosus Willd. Leaf. Research Journal of Pharmacy and Technology. 2013; 6(12):1387-1390.
14. Dalvi SS. Nadkarni PM. Gupta KC. Effect of A. racemosus (Shatavari) on Gastric Emptying Time in Normal Healthy Volunteers. Journal of Postgraduate Medicine. 1990; 36(2):91–94. PMID: 2097375
15. Kushwah P. Ghulaxe SP. Mandloi N. Singh S. Patel R. Review on Medicinal value of Asparagus racemosus in Woman's. Research Journal of Pharmacy and Technology. 2018;11(1):418-420. DOI: 10.5958/0974-360X.2018.00077.X
16. Jayasri MA. Radha A. Mathew TL. α-Amylase and α-Glucosidase Inhibitory Activity of Costus pictus D. Don in the Management of Diabetes. Journal of Herbal Medicine and Toxicology. 2009; 3(1):91-94. Corpus ID: 86321442
17. Gallagher AM. Fatt PR. Duffy G. Abdel-Wahab YHA. The effects of Traditional Anti-diabetic Plants on In Vitro Glucose Diffusion. Nutrition Research. 2003; 23(3):413-424. DOI:10.1016/S0271-5317(02)00533-X
18. Cirillo VP. Wilkins PO. Anton J. Sugar transport in a psychrophilic yeast. Journal of Bacteriology. 1963; 86(6):1259-64. DOI: 10.1128/jb.86.6.1259-1264.1963
19. Ou S. Kwok KC. Li Y. Fu L. In Vitro Study of Possible Role of Dietary Fiber in Lowering Postprandial Serum Glucose. Journal of Agricultural Food Chemistry. 2001; 49(2): 1026-1029. DOI: 10.1021/jf000574n
20. Hayes PY. Jahidin AH. Lehmann R. Penman K. Kitching W. De Voss JJ. Structural Revision of Shatavari I and IV, the Major Components from the Roots of Asparagus racemosus. Tetrahedron Letters. 2006; 47:6965-6969. DOI: 10.1016/j.tetlet.2006.07.121
21. Singh J. Tiwari HP. Chemical Examination of Roots of Asparagus racemosus. Journal of Indian Chemical Society. 1991; 68(7): 427-428.
22. Jay B. Sagar B. Pankaj N. Savalia V. Devang P. Isolation and Characterization of Marker Compound for Detecting Adulteration of Chlorophytum Species in Asparagus racemosus. Research Journal of Pharmacy and Technology. 2021; 14(2):800-802. DOI: 10.5958/0974-360X.2021.00140.2
23. Revathi R. Julius A. Effect of Insulin Resistance in Obese Polycystic Ovarian Disease. Research Journal of Pharmacy and Technology. 2017; 10(7):2160-2162. DOI: 10.5958/0974-360X.2017.00381.X
24. White MF. The IRS-Signaling System: A Network of Docking Proteins that Mediate Insulin and Cytokine Action. Recent Programme Hormonal Research. 1998; 53: 119–138. PMID: 9769706
25. Saltiel AR. Diverse Signaling Pathways in the Cellular Actions of Insulin. American Journal of Physiology. 1996; 270(3 Pt 1): E375–378. DOI: 10.1152/ajpendo.1996.270.3.E375
26. Cortón M, Botella-Carretero JI, Benguria A, Villuendas G, Zaballos A, San Millán JL, Escobar-Morreale HF et al Differential Gene Expression Profile in Omental Adipose Tissue in Women with Polycystic Ovary Syndrome. The Journal of Clinical Endocrinology and Metabolism. 2007; 92 (1): 328–337. DOI: 10.1210/jc.2006-1665
27. Li T. Mo H. Chen W. Li L. Xiao Y. Zhang J. Li X et al Role of the PI3K-Akt Signaling Pathway in the Pathogenesis of Polycystic Ovary Syndrome. Reproductive Science. 2017; 24(5): 646-655. DOI: 10.1177/1933719116667606
28. Welsh GI. Hale LJ. Eremina V. Jeansson M. Maezawa Y. Lennon R. Pons DA et al Insulin Signaling to the Glomerular Podocyte is Critical for Normal Kidney Function. Cell Metabolism. 2010; 12 (4):329–340. DOI: 10.1016/j.cmet.2010.08.015
29. Karthik VP. Suresh P. David DC. In Vitro Hydrogen Peroxide Scavenging Activity and Alpha Amylase Inhibitory Activity of Croton tiglium Extract. Research journal of Pharmacy and Technology. 2019;12(6):3045-3047. DOI: 10.5958/0974-360X.2019.00515.8
30. Vadivelan R. Gopala Krishnan R. Kannan R. Antidiabetic Potential of Asparagus racemosus Willd Leaf Extracts through Inhibition of α-Amylase and α-Glucosidase. Journal of Traditional Complementary Medicine. 2019; 9(1):1–4. DOI: 10.1016/j.jtcme.2017.10.004
31. Hannan JM. Marenah L. Ali L. Rokeya B. Flatt PR. Abdel-Wahab YH. Insulin Secretary Actions of Extracts of Asparagus racemosus Root in Perfused Pancreas, Isolated Islets and Clonal Pancreatic Beta-Cells. Journal Endocrinology. 2007; 192(1):159-168. DOI: 10.1677/joe.1.07084
32. Archit R. Gayathri M. Punnagai M. An In Vitro Investigation into the Mechanism of Anti-Diabetic Activity of Selected Medicinal Plants. International Journal of Drug Development and Research. 2013; 5 (3):221-226. Corpus ID: 75576809
33. Hannan JM. Ali L. Khaleque J. Akhter M. Flatt PR. Abdel-Wahab YH. Anti-hyperglycemic Activity of Asparagus racemosus Roots is Partly Mediated by Inhibition of Carbohydrate Digestion and Absorption, and Enhancement of Cellular Insulin Action. British Journal of Nutrition. 2012; 107(9):1316–1323. DOI: 10.1017/S0007114511004284
34. Pitchaipillai R. Ponniah T. In Vitro Antidiabetic Activity of Ethanolic Leaf Extract of Bruguiera Cylindrica L. – Glucose Uptake by Yeast Cells Method. International Biological Biomedical Journal. 2016; 2 (4):172-175. Corpus ID: 55875703
35. Corbould A. Chronic Testosterone Treatment Induces Selective Insulin Resistance in Subcutaneous Adipocytes of Women. Journal Endocrinology. 2007; 192(3):585–594. DOI: 10.1677/joe.1.07070