Synopsis of the thesis on

Potential of non-polar fraction of *Aloe barbadensis* Mill. gel extract in management of Polycystic Ovarian Syndrome

Submitted to

The Maharaja Sayajirao University of Baroda

For the degree of

Doctor of Philosophy (Ph.D.) in Biochemistry

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August, 2018

Synopsis

Introduction:

Polycystic Ovary Syndrome (PCOS) is an exceedingly prevalent metabolic disorder and possibly constitutes the most frequently encountered endocrinopathy to affect women. PCOS is a frequent medical condition characterized by both metabolic and reproductive disorders, affecting 4-26% of women at their reproductive age (Chatterjee and Bandyopadhyay, 2020). The clinical manifestations of this highly heterogeneous disease include amenorrhea, hirsutism, obesity, hyperinsulinemia, hyperandrogenism, polycystic ovaries via ultrasound, and it attributes three fourth of the ovulatory infertility (Kini, 2012). The above-mentioned conditions are very severe and can lead to increased incidences of obesity, diabetes, endometrial cancer, ovarian cancer, hypertension, and heart disease in PCOS women (Moran et al., 2010; Wild et al., 2000; Dumesic and Lobo, 2013). Different pharmaceutical treatments have been proposed for PCOS. Mostly, the available medication is to treat the symptoms of PCOS and to reduce the severity of the disorder and its maintenance. Till today no cure for this disorder is found, but there are several ways to maintain this condition without any further increase in severity.

Treatment of PCOS involves administration of steroid analogues and insulin sensitizers like Metformin, Clomiphene Citrate and Rosiglitazone;however, the use of these synthetic drugs gives rise to several side effects. So, scientists are searching for herbal therapies for treatment of PCOS as they are less invasive, less expensive and equally effective in the management of PCOS.A variety of bioactive molecules from several medicinal plants have been studied in context of PCOS, some of which being saponins from*Panax ginseng* (Pak *et al.*,2005), phytoestrogens from *Cimicifuga racemosa* (Kamel *et al.*,2013), phytosterols and phenolics from Punica granatum (Hossein,2015) and *Aloe vera* gel (Maharjan et al., 2010).

Aloe barbadensis Miller: commonly known as *Aloe vera* and belongs to family Liliaceae. Traditional knowledge of Ayurveda and Siddha has several evidences which substantiate the effectiveness of *Aloe vera*, also called as kattrali, kani or kumari towards management of female reproductive system and its associated disorders like PCOS (Nadkarni, 1976; Risvan et al., 2017; Sahu et al., 2013). PCOS, being a metabolic syndrome, is characterized by glucose intolerance, insulin resistance and dyslipidemia. There are several evidences that have proved *Aloe vera* gel is an efficient modulator of metabolic status by exhibiting hypoglycemic, anti-dyslipidemic, antioxidant and anti-inflammatory properties (Desai et al., 2012; Tanaka et al.,

2006; Misawa et al., 2008; Misawa et al., 2012). The varied pharmacological properties of *Aloe vera*gel is due to its abundant phytochemicals such as polysaccharides, glycosides, flavonoids, carbohydrates, coumarins, tannins, chromones, alkaloids, anthraquinones, organic compounds, pyrones, phytosterols, anthrones, fatty acids, sterols, terpenoids, hormones, vitamins, proteins, and mineral constituents (Nalimu et al., 2021; Kar and Bera, 2018; Radha and Laxmipriya, 2015). Though its ethnopharmacological use has been documented in traditional medicine system, its thorough scientific evidence is lacking.

In this context, data from our lab demonstrated that *Aloe vera* gel (10mg dry weight daily for 60 days) could restore ovarian structure-function and decrease co-morbidities like hyperglycemia and dyslipidemia in PCOS rat model (Maharjan et.al., 2010; Radha et al., 2014; Desai et al., 2012; Radha and Laxmipriya, 2015). Further, it is interesting to note that PCOS rats treated with *Aloe vera* gel (AVG) before conception could increase implantation rate, leading to healthier pups with few or no resorptions, suggesting that AVG is a good pre-conceptive agent and help in management of complications associated with women (Radha and Laxmipriya, 2016b). Further, solvent based extraction of AVG demonstrated that oral administration of non-polar petroleum ether extract (NPE) (25 µg/kg body weight for 60 days) in Letrozole induce PCOS rat model could affectively improve the reproductive and metabolic complications associated with PCOS. The observed efficacy was attributed to the presence of fatty acids, phytosterols and terpenoids in the NPE, which acted at various molecular targets leading to improve the ovarian structure- function along with metabolic modulation (Radha and Laxmipriya, 2016a).

Since plant extracts are typically a mixture of different types of bioactive compounds or phytochemicals with different polarities, separating them remains a significant challenge in the identification and characterization of bioactive compounds. The varied phytochemicals present in the extract may potentiate undesirable side-effects. Moreover, certain plant-derived compounds are effective in combination with others, while others are active as single entities. The current advancement in science has made it possible for the isolation of phytochemicals and studying their therapeutic potential individually or in combination in order to understand their key molecular targets. Thereby, isolation of the non-polar phytocomponents present in *Aloe vera* gel by chromatographic techniques help us to identify their molecular targets by using *"in-silico", "in-vitro"* and *"in-vivo"* approaches. ***Hence, it can be hypothesized that***

non-polar phytocomponents present in Aloe vera gel may act as potential therapeutic alternative for reproductive and metabolic disturbances in PCOS.

Aim of the study

In light of the above literature, the aim of the present study was to isolate the bioactive non-polar phytocomponent/s of *Aloe barbadensis* Mill, gel and elucidate their potential molecular targets using *"in-silico", "in-vitro"* and *"in-vivo"* approaches; with defining therapeutically possible molecular mechanism that be directed towards the better management of PCOS and its associated metabolic co-morbidities.

Specific Objectives:

Major objectives of the present study are –

I. To isolate and characterize the non-polar phytocomponents of *Aloe vera* gel and evaluate their pharmacokinetics, distribution and pharmacodynamics in rats.

II. To identify the targets of the isolated phytocomponents of non-polar fraction of *Aloe vera* gel Extract using "*in-silico*" approach and its validation.

III. To evaluate the role of isolated phytocomponents of non-polar fraction of *Aloe vera* gel Extract in PCO-like ovarian cellular models.

IV. To evaluate the role of isolated phytocomponent/s of non-polar fraction of *Aloe vera* gel Extract in Letrozole induced PCOS mouse model.

Hypothesis:

We hypothesize that non-polar phyto-components of *Aloe vera* gel can manage the PCOS pathology by modulating the key steroidogenic and metabolic targets.

Significance:

This study will be helpful in identification of the bioactive components of *Aloe-vera* gel as potential therapeutic alternative for reproductive and metabolic disturbances in PCOS. It will elucidate the physiological mechanisms for efficacy of the isolated bioactive components. **Thereby, this study will be helpful in identification of a new and naturally derived drug**

target and add to its overall potential and economic viability at national and international level.

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II. To identify the targets of the isolated phytocomponents of non-polar fraction of *Aloe vera* gel Extract using "*in-silico*" approach and its validation.
III. To evaluate the role of isolated phytocomponents of non-polar fraction of *Aloe vera* gel Extract in PCO-like ovarian cellular models.
IV. To evaluate the role of isolated phytocomponent/s of non-polar fraction of *Aloe vera* gel Extract in Letrozole induced PCOS mouse model.

Summary of the work done

I. To isolate and characterize the non-polar phytocomponents of *Aloe vera* gel and evaluate their pharmacokinetics, distribution and pharmacodynamics in rats.

In order to isolate the bioactive non-polar phytochemicals from AVG, the petroleum ether extract of AVG was sub-fractionated by column chromatography to derive 5 partially purified isolates- LP1, LP2, LP3, LP4 and LP5. The phytoconstituents of the partially purified isolates was confirmed by GC/MS analysis followed by comparing with the NIST Library. LP1, LP2, LP3, LP4 and LP5 were found to contain n-Hexadecanoic acid, Cholesta-3,5-diene, Campesterol acetate, b-Sitosterol and Stigmasterol acetate with an abundance of 97.07%, 96.04%, 94.03%, 92.45% and 87.49% respectively, which was also confirmed by performing reverse-phase HPLC by means of running respective standards.

Apart from the phytochemical analysis, pharmacokinetic and pharmacodynamic assessment was performed in rats to understand how the phytochemicals are absorbed, distributed, metabolised and excreted from the body. A potent molecule must reach its target in the body in sufficient concentration and stay there in a bioactive state long enough for the predicted biologic activities to occur for it to be effective as a medication (Daina et al., 2017). Based upon GC/MS analysis, it was observed that amongst the different non-polar phytocompounds, the absorption of n-Hexadecanoic acid, Campesterol acetate, b- sitosterol, Cholesta-3,5-diene and Stigmasterol acetate in the plasma was maximum within 5 hours of oral administration of

100 mg/kg body weight of Petroleum ether extract to the animals. In addition to this, the above-mentioned phytochemicals exhibited greater affinity towards steroidogenic active tissues such as ovaries, adrenal, uterus and also liver. However, other tissues that play an important role in the etiopathology of PCOS like skeletal muscles, kidney, hypothalamus, pituitary also demonstrated the presence of these phytochemicals, but the concentration was very low. In spite of having low oral bioavailability, the non-polar phytocompounds isolated from *Aloe vera* gel exhibited good pharmacodynamic properties, wherein, they reduced the testosterone levels and increased the estradiol and progesterone levels in the animals within 2.5 hours of treatment. Results suggest that fatty acid such as n-Hexadecanoic acid and phytosterols such as Campesterol acetate, beta-sitosterol, Stigmasterol acetate or its metabolite like Cholesta-3,5-diene may be responsible for such response**.**

II. To identify the targets of the isolated phytocomponents of non-polar fraction of *Aloe vera* gel Extract using *"in-silico"* approach and its validation

In order to elucidate the molecular targets and the magnitude of interaction with the steroidogenic and metabolic targets, through which the major components of partially purified non-polar phytocomponents (PPNPP) of *Aloe vera* gel act, an "in-silico" molecular docking experiment was performed using the Glide tool developed by Schrödinger. The docking score, binding free energy, and hydrogen bonds produced with the surrounding amino acids were all utilised to predict the binding affinities and correct alignment inside the active sites of the key steroidogenic and metabolic targets, such as the Follicle Stimulating Hormone Receptor (FSHR), Steroidogenic Acute regulatory protein (StAR), 3-beta hydroxysteroid dehydrogenase (3b-HSD), Aromatase, Estrogen Receptor alpha, Estrogen Receptor beta, Androgen receptor, Progesterone receptor, and Phosphorylated Insulin Receptor tyrosine kinase. n-Hexadecanoic acid, Cholesta-3,5-diene, Campesterol acetate, b-Sitosterol and Stigmasterol acetate, which are the major phytochemical constituent of LP1, LP2, LP3, LP4 and LP5 respectively were considered as the ligands for the "in-silico" studies. Results demonstrate that Campesterol acetate (a significant component of LP3) has the highest affinity for important steroidogenic targets such as the Progesterone receptor, Steroidogenic Acute Regulatory protein, and Aromatase, with docking scores of -9.988, -8.312, and -6.913, respectively. With docking scores of -7.166 and -6.512, respectively, the Estrogen Receptor beta and 3-beta hydroxysteroid dehydrogenase were shown to have excellent interactions with beta-Sitosterol (LP4) and Stigmasterol acetate (LP5). With docking scores of -7.419 and -3.205, n-Hexadecanoic acid

(LP1) was revealed to dock with Androgen Receptor and phosphorylated Insulin Receptor tyrosine kinase, respectively.

Results have demonstrated that the docking efficiency and H-bond forming capacity of Campesterol acetate (major constituent of LP3) and beta-Sitosterol (major constituent of LP4) are more towards steroidogenic targets like StAR, Aromatase, ER-b and PR. On the other hand, n-Hexadecanoic acid, which was the major component of LP1, was found to strongly interact with Androgen Receptor by forming Hydrogen bonds within the DNA-binding domain of it. LP1 was also found to interact with p- Insulin receptor tyrosine kinase with low docking score, but very low potential energy of binding, suggesting that LP1 confers good affinity towards the target. Furthermore, using the Swiss ADME programme, which predicts physically significant and physiochemical characteristics of prospective therapeutic compounds, assessments of the pharmacokinetic parameters of Absorption, Distribution, Metabolism, and Excretion (ADME) of the non-polar phytochemicals were computed. Our results suggest that all the non-polar phytochemicals possessed desired properties and could be developed into potential drug candidates. The phytochemical poses minimal potential for adverse effects when consumed orally because of their low bioavailability. For the first time, the present study has revealed the "drug likeness" properties of non-polar phytochemicals isolated from *Aloe vera* gel and their potential to modulate important steroidogenic and metabolic targets using "in-silico" studies.

Validation of the results obtained in the "in-silico" study was performed by incubating the phytochemicals with the KGN cell-line. KGN cell line is a steroidogenic human ovarian granulose-like tumour cell line that has been used to study steroidogenesis, cell proliferation, and FSHR-coupled signalling in human granulosa cells (Havelock, 2004). Furthermore, KGN cell are capable of secreting estrogen and progesterone (Nishi et al., 2001). Results from the current bioassay study demonstrates the anti-androgenic potential of LP1, and estrogenic, progestogenic nature of LP3. LP1 and LP3 elicit their response by modulating the gene expression of gonadotropin receptors, steroid receptors as well as other key steroidogenic marker proteins. Several studies over the past decade have demonstrated similar bioactive potential of phytosterols, terpenoids and fatty acids isolated from other dietary sources in birds (Qasimi et al., 2018), fishes (Sharpe et al., 2006; Palermo et al., 2013), rodents (Wang et al., 2018), human adrenocortical H295R cells (Ohno et al., 2002) and pig-derived granulosa cells (Santini et al., 2009). However, reporting such bioactivity for these non-polar phytochemicals

isolated from *Aloe vera* gel is novel and holds immense potential for drug development against female endocrinopathies like PCOS.

The steroidogenic and metabolic regulatory potential of LP1 and LP3 were proven in KGN cell-line under normal physiological conditions. However, it would be interesting to study their bioactive potential in a pathological condition like PCOS. In this context, it is to be noted that the granulosa cells, which are the major ovarian cells, are prone to damage by presence of hyperandrogenism and hyperinsulinemia conditions, as observed in case of PCOS (Dey et al., 2021; Belani et al., 2018). The granulosa cells are the most important ovarian cell as the support the growing oocyte, proliferates, and produces sex hormones and a variety of growth factors, all of which are necessary for follicle development (Tu et al., 2019).

III. To evaluate the role of isolated phytocomponents of non-polar fraction of *Aloe vera* gel Extract in PCO-like ovarian cellular models.

Firstly, we developed *"in-vitro*" model of PCO using primary culture of rodent derived luteinized granulosa cells and human derived immortal granulosa cell-line- KGN. Co-administration of 0.1 mIU/mL insulin and 50ng/mL DHT to the primary culture of LGCs and 2.0 mIU/mL insulin and 100 ng/mL DHT to the KGN cell line, respectively, effectively regulated the key genes involved in steroidogenesis, thereby leading to abnormal steroid hormone secretion by the cells. The observed effects were similar to that observed in the granulosa cells of PCOS patients (Wickenheisser et al., 2005; Pigny et al., 2003; Dewailly et al., 2003; Karkanaki et al., 2011; Chaves et al., 2012; Yang et al., 2015; Doldi et al., 2000). The establishment of a novel *"in-vitro*" PCO model is remarkable and has enormous promise for investigating precise downstream cellular signalling as well as therapeutic target screening for ovarian dysfunctions like PCOS. There have been no previous studies that involved screening phytochemicals for their steroidogenic modulatory potential in a PCO-like ovarian microenvironment. The impact of LP1 and LP3 on the regulation of steroidogenic targets and hormone production by PCO-like KGN cells was the emphasis of this study. The gene expression of steroidogenic targets Luteinizing Hormone Receptor (Lhr), Steroidogenic acute regulatory protein (Star), Aromatase (Cyp19a1), Androgen Receptor (Ar), and Progesterone Receptor (Pgr) was competently modulated by LP1 and LP3, as well as their respective standards. ***This is the first study to demonstrate the bioactivity of non-polar phytocompound/s of Aloe vera gel in an "in-vitro" PCO- like model towards restoration of dysregulated steroidogenesis at the molecular level.***

Though, cell- based bioassays are the most promising tool for screening of numerous phytochemicals simultaneously (Moore et al., 2014), *"in-vitro"* studies have limitations since they can't simulate how a pharmaceutical drug interacts within a complex and dynamic ecosystem like human body, where multiple signalling pathways work in harmony to give rise to a certain phenotype. *"In-vitro*" studies may find it challenging to forecast the complexity of possible interactions as a result of this. On the other hand, *"in-vivo"* studies can provide a better understanding of the molecular targets of the drugs and their potential interactions with different organs of the body, which can improve its predictions of safety, toxicity, and efficacy. Considering PCOS is a heterogeneous disease that affects various organ systems and has substantial metabolic and reproductive symptoms (Williams et al., 2016), evaluating bio-isolate effectiveness in an *"in vivo"* system is critical.

IV. To evaluate the role of isolated phytocomponent/s of non-polar fraction of *Aloe vera* gel Extract in Letrozole induced PCOS mouse model.

With this background, the current study focused at the effects of LP1 and LP3 in a Letrozole-induced PCOS mouse model, as well as hormonal and metabolic pathways for managing PCOS pathology and its comorbidities. Letrozole (an aromatase inhibitor) has been shown to be effective in instigating PCOS in animals (Kafali et al., 2004). It works by inhibiting aromatase, resulting in a lower conversion of androgens to estrogens and an excess of androgens in the ovary (Garcia-Velasco et al., 2005). The mouse model of PCOS was generated with letrozole (0.5 mg/kg/day orally for 21 days) and showed abnormal clinical manifestations (Dey et al., 2017). The PCOS group had a substantial elevated body weight. It has previously been shown that an increase in abdominal fat storage is linked to an increase in body weight and may cause adipocyte malfunction and insulin resistance in PCOS patients (Goodarzi et al., 2011). Furthermore, letrozole-treated mice had glucose intolerance, higher fasting insulin levels, higher HOMA-IR values, and higher circulating triglyceride levels. Previous research has shown similar markers of metabolic imbalance (Kauffman et al., 2015; Kelley et al., 2016). According to Desai et al., 2012, the insulin resistance and poor glucose tolerance caused by letrozole are mostly attributable to increased testosterone concentrations.

In addition to this, administration of letrozole caused reproductive irregularities, as evidenced by a halted estrus cycle during the diestrus stage, increased testosterone levels, and decreased progesterone levels. Furthermore, ovarian sections revealed numerous peripheral cystic follicles, which are etiological feature of PCOS. These findings are comparable to those found

in previous studies (Rajan and Balaji, 2017; Yang et al., 2018a; Yang et al., 2018b). As a result, this model is appropriate for exploration of both reproductive and metabolic aspects of the condition, and it may be utilised to better understand the etiopathology and assess the bioactivity of the isolated non-polar phytochemicals.

Treatment of PCOS mice with LP3 and CA resulted in substantial weight loss, increased glucose tolerance, lower fasting insulin levels, and lower HOMA-IR readings, which was comparable with that of *Aloe vera* gel and Petroleum ether extract of *Aloe vera* gel treated groups. It's possible that non-polar phytocompounds found in *Aloe vera* gel could decrease glucose resistance through regulating glucose homeostasis, increasing insulin production, and potentiating glucose absorption by insulin. This supports the hypothesis that *Aloe barbadensis* isolated bioactives might be used as a metabolic modulator (Desai et al., 2012). Furthermore, these therapies may be beneficial in lowering the levels of circulating triglycerides in PCOS animals. Studies by Alinejad-Mofrad et al., (2015); Maharjan et al., (2010) and Desai et al., (2012) have reported similar findings. Phytosterols found in *Aloe vera* gel have been shown to be effective in controlling glucose and lipid metabolism in rats in a number of investigations (Tanaka et al., 2006; Misawa et al., 2008; Misawa et al., 2012).

When compared to control animals, PCOS animals displayed an irregular estrus cyclicity, presence of numerous peripheral cysts, higher testosterone levels, and lower progesterone levels. Treatment of the PCOS animals with *Aloe vera* gel, petroleum ether extract of *Aloe vera* gel and LP3 restored the ovarian structure-function. The observed bioactivity of LP3 was better than that of Metformin, which is the most commonly used treatment for PCOS. Supporting our findings, Demirel and his colleagues (2016) observed that tocopherol, squalene, b-sitosterol, campesterol, and stigmasterol contained in Corylus avellana seed oil produced a substantial decrease in testosterone levels and restored ovarian function in PCOS rats. In PCOS rats, Vitex agnus-castus fruit extract had an antiandrogenic impact via enhancing aromatization, resulting in reduced testosterone levels (Jelodar and Askari, 2012). Because abnormally high testosterone levels contribute to the development of PCOS, testosterone downregulation post LP3 therapy might help with managing the reproductive complications associated with PCOS. Recent research has focused on the role of campesterol and stigmasterol as progesterone precursors (Janeczko, 2012; Tarkowská, 2019), suggesting that plant sterols may have the ability to influence hormone metabolism.

The results of this investigation showed that LP1 had mainly an anti-androgenic activity. LP3, on the other hand, was shown to be more effective than LP1 at regulating the steroidogenic and

metabolic parameters linked to PCOS. The mode of action of LP3, a partly pure non-polar phytochemical produced from *Aloe vera* gel, might be owing to its modulatory impact on steroid receptor transcription, primarily functioning as an anti-androgenic and progestenic agent. It aided in the restoration of ovarian shape and function in Letrozole-induced PCOS mice by regulating the hormonal environment. Furthermore, therapy with LP3, AVG, and PE reduced metabolic dysfunction associated with PCOS, such as glucose intolerance, insulin resistance, and dyslipidaemia. Surprisingly, LP3 was shown to be as effective as AVG and PE in treating reproductive and metabolic problems in Letrozole-induced PCOS mice, without any toxicity, suggesting that oral administration of LP3 (0.5 g/kg/day) for 60 days is sufficient for PCOS therapy. Paradoxically, the therapeutic potential of LP3 was higher than that of metformin, the most often recommended medication for PCOS. It is also interesting to note these isolated bioactives were safe as they did not show any sign of toxicity in their preclinical trial as evident in our study.

Conclusion:

Overall, the current study supports the hypothesis that bioactive non-polar phytocomponents present in *Aloe vera* gel act as potential therapeutic alternatives for management of reproductive and metabolic disturbances in PCOS. Taken together, the data from *"in-silico", "in-vitro"* and *"in-vivo"* studies provide the evidence that LP3 (comprising of 94.03% Campesterol acetate) is the bioactive non-polar phytocompound of *Aloe vera* gel that can be used to treat PCOS and its associated reproductive and metabolic comorbidities with minimum side effects. Also, the mechanism of action of LP3 is by regulating the key steroidogenic and metabolic targets, thereby improving the ovarian structure-function and the metabolic status in a multi etiological endocrine pathology like PCOS. Further, detailed molecular signaling involved in the observed bioactivity of LP3 needs to be explored. Also, this is first study wherein we have identified the targets of the partially purified non polar phytocomponents of *Aloe vera* gel. Hence, they could be considered for future drug development. ***The present study attempted to add a new facet with scientific explanation to Aloe vera plant, that has been traditionally used in Indian system of ancient medicine; thus, adding its value for commercial exploitation.***

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(From thesis)

1. **Dey, A.,** Mehta, I., Ghosh, P., & Nampoothiri, L. (2021). Synergistic Interplay of Hyperandrogenism and Hyperinsulinism on Primary Culture of Luteinized Granulosa Cells–an "in-vitro" Model Mimicking Ovarian Microenvironment of Poly-Cystic Ovary Syndrome (PCOS). Journal of Endocrinology and Reproduction, 24(1), 53-65.DOI: 10.18311/jer/2020/26764.

2. **Arpi, D.,** & Laxmipriya, N. (2019). Nutraceuticals as Therapeutic Agents for Management of Endocrine Disorders - Sources, Bioavailability and Mechanisms Underlying their Bioactivities. Acta Scientific Nutritional Health. 3.2: 97-109.

3. **Arpi Dey**, Radha Maharjan and Laxmipriya Nampoothiri (2017). Phytosterols isolated from *Aloe barbadensis* Mill., restore reproductive and metabolic complications in Letrozole-induced PCOS mouse model. *J Diabetes Metab*, 8:10 (Suppl) DOI: 10.4172/2155-6156-C1-073.
4. **A Dey**, S Vasoya, L Nampoothiri (2017). Pharmacokinetics and bioavailability of non-polar phytocomponents of *Aloe vera* gel and their role as an endocrine modulator in letrozole induced PCOS rat model. *BioScientifica Endocrine Abstracts* 49. EP1117 | DOI: 10.1530/endoabs.49. EP1117.
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(From collaborative work)

1. Laxmipriya, N., Prashant, Sudra., **Arpi, D.**, Shivani, D., Azazahemad A. K., Satyanshu, K., Tushar, D., Raghuraj, S.,&Premlata, K. (2021). Fruit juice of Garcinia indica Choisy modulates dyslipidemia and lipid metabolism in cafeteria diet-based rat model. *Ann. Phytomed.,* 10(1):78-85.DOI: http://dx.doi.org/10.21276/ap.2021.10.1.8.

Conference Proceedings:

Abstracts published in meetings/conferences

1. **Arpi Dey**, Ishita Mehta, Priyanka Oshin, Priyanka Ghosh, Radha Maharjan, Shivani Dhadhal & Laxmipriya Nampoothiri. *"Non-polar phytocomponents of Aloe barbadensis Mill. act as potential therapeutic alternative for Polycystic Ovarian Syndrome by targeting steroidogenic and metabolic receptors"* at Global Conference on Reproductive Health with Focus on Occupational, Environmental and Lifestyle Factors and 29th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility. New Delhi, India.22nd-24thFebruary 2019.
2. **Arpi Dey**, Radha Maharjan and Laxmipriya Nampoothiri. *"Phytosterols isolated from Aloe barbadensis Mill., restore reproductive and metabolic complications in Letrozole-induced PCOS mouse model"* at 23rdInternational Conference on Herbal and Alternative Remedies for Diabetes and Endocrine Disorders. Bangkok, Thailand.2nd - 4thNovember 2017
3. **Arpi Dey**, Shweta Vasoya and Dr. Laxmipriya P. Nampoothiri. *"Pharmacokinetics and bioavailability of Non-polar phytocomponents of Aloe vera gel and their role as an endocrine modulator in Letrozole induced PCOS rat model"* at 19thEuropean Congress of Endocrinology. Lisbon, Portugal. 20th-23rdMay 2017.
4. **Arpi Dey** and Laxmipriya Nampoothiri. *"Bioassay guided isolation and identification of steroid modulating phytochemicals from Aloe barbadensis Mill. Gel"* at 4thInternational Congress for Ethnopharmacology, India, SFEC 2017, Bardoli, India.23rd-25thFebruary, 2017.
5. Radha Maharjan, **Arpi Dey** and Nampoothiri L. *"Unraveling the molecular targets of Aloe vera gel towards management of female fertility in Letrozole induced PCOS Rat Model"* at International Symposium on Integrative Physiology & Comparative Endocrinology and 34th Annual Meeting of the Society for Reproductive Biology and Comparative Endocrinology (SRBCE), Department of Zoology, Banaras Hindu University, Varanasi, India. 12th-14thFebruary 2016.
6. Laxmipriya P. Nampoothiri, Radha Maharjan and **Arpi Dey** *"Implication of. non-polar phyto-components of Aloe vera gel in management of Polycystic Ovarian Syndrome"* at European Congress of Endocrinology (ECE), Dublin, Ireland, 16th-20thMay, 2015.
7. **Arpi Dey**, Shivani Dhadhal and Laxmipriya Nampoothiri. "*Comparative evaluation of Non-Polar extracts of Aloe vera gel in management of Polycystic Ovarian Syndrome."* at International Conference on Bioactive Chemicals for reproduction and Human

Health & 33rd Annual Meeting of the Society for Reproductive Biology and Comparative Endocrinology; Davangere, India. 26th-28thFebruary 2015.

8. **Dey A**., Chaudhary M., Soni R., Patel B. and Nampoothiri L.P. *"Ovarian structure-function alterations in L-methionine treated hyper-homocysteinemia rat model"* at National Conference on Emerging trends in Biochemical Sciences; Vadodara, India. 29th -31stDecember 2014.
9. **Dey A.** and Nampoothiri L.P. *"Letrozole induced dose and time- dependent development of a Polycystic Ovarian Syndrome mouse model"* at International Conference on Recent trends in Biomedical Sciences & 32nd Annual Meeting of Society for reproductive Biology & Comparative Endocrinology, Tiruchirapalli, India. 7th-9thJanuary 2014.

Academic Achievements and Awards:

1. Journal of Endocrinology (JOE) Travel award 2017 for attending 19th European Congress of Endocrinology held at Lisbon, Portugal. May 20-23 2017.
2. Best poster award (First prize) at International Symposium on Integrative Physiology & Comparative Endocrinology and 34th Annual Meeting of the Society for Reproductive Biology and Comparative Endocrinology (SRBCE), Department of Zoology, Banaras Hindu University, Varanasi. 12th-14th February 2016.
3. Prof. N.J. Chinoy best paper award for poster presentation at International Conference on Recent trends in Biomedical Sciences & 32nd Annual Meeting of Society for reproductive Biology & Comparative Endocrinology, Tiruchirapalli during 7th-9th January 2014.

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