Implication of non polar phyto-components of *Aloe vera* gel in management of Polycystic Ovarian Syndrome

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Introduction

- Polycystic Ovarian Syndrome (PCOS) is recognized as the most common endocrinopathy of women with increased androgen synthesis, disrupted folliculogenesis and insulin resistance .
- Current therapies are oral contraceptive pills and insulin sensitizers, which produces various side effects upon prolong usage.
- Thereby, it was worthwhile to screen herbal alternative that could manage such a complex syndrome.
- A popular herb, *Aloe barbadnesis* Mill., reported for several medical efficacies, one being anti-diabetic property.
- In this context, we have clearly implicated that *Aloe vera* gel has potential to act as fertility agent (Maharjan *et al*., 2010, 2014, 2015) and manage PCOS associated complications (Desai *et al.*,2012).
- "*In vitro* " studies have shown that Non polar fraction *of Aloe vera* gel can modulate steroidogenic enzymes.
- Thereby, our interest was to elucidate the molecular targets by which non-polar fractions of *Aloe vera* gel (AVG) could manage PCOS phenotype.

Objectives

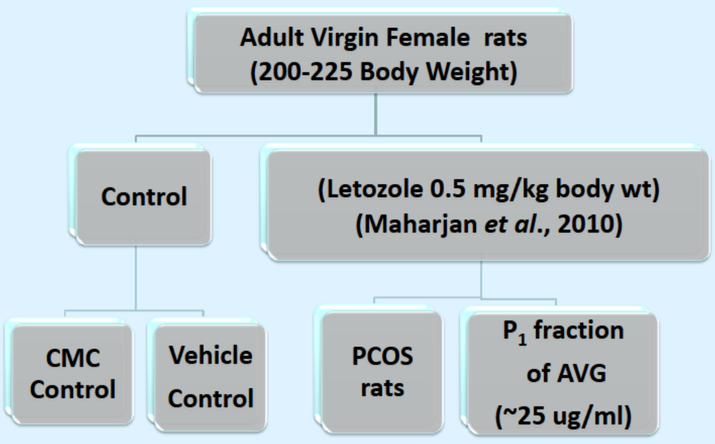
⇒ Development of letrozole (0.5 mg/kg body weight) induced PCOS rat model and validation of model.

⇒ Partially purification of *Aloe vera* gel based on polarity gradient method and phytochemical analysis of non polar fraction of gel extract.

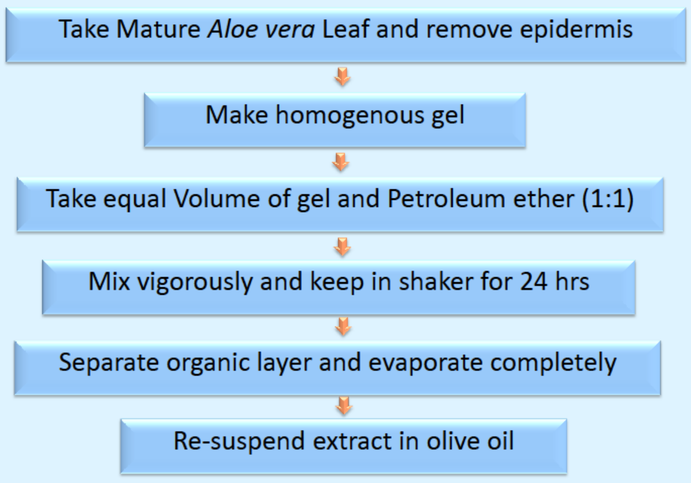
⇒ Effect of non polar fraction of *Aloe vera* gel on letrozole induced PCOS rat model- "*In vivo*" study.

Methods

A. Plan of work
Rodent PCOS model



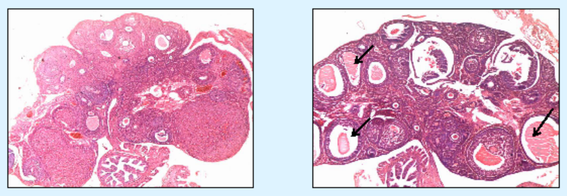
B. Extraction Method of *Aloe vera* gel



Results

Validation of PCOS rat model

1. Histological analysis

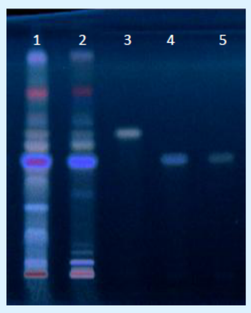


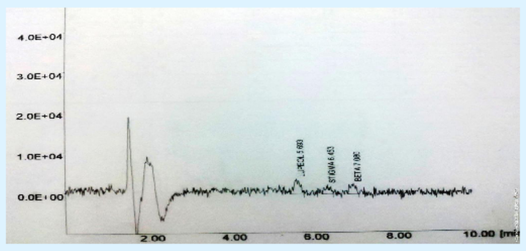
2. Hormonal profile

GROUPS	Testosterone (ng/ml)	Estradiol (ng/ml)	Progesterone (ng/ml)	Insulin (μIU/ml)	HOMA-IR
CONTROL	0.41±0.08	0.75±0.1	46.0±3.0	7.33±1.66	1.19±0.22
PCOS	1.1±0.15**	0.34±0.2*	27.±6.24	17.6±0.8***	4.2 ±0.12***

*P<0.05; **P<0.01; ***P<0.001 as compared to Control group.

Phytochemical analysis of non polar extract of *Aloe vera* gel





HPLC Analysis

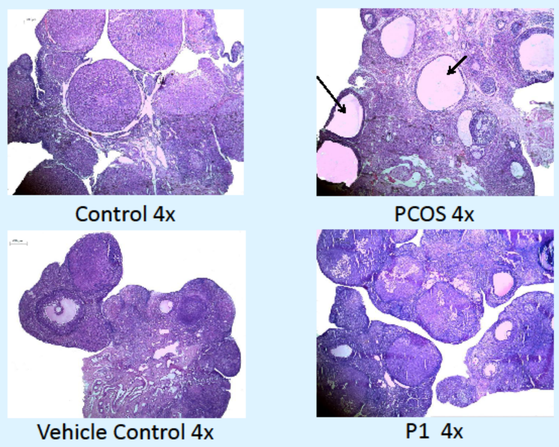
HPTLC Analysis

Track 1: P_1 fraction
Track 2: Fresh Aloe
Track 3:Lupeol 50 ppm
Track 4: β Sitosterol 50 ppm
Track 5: Stigmasterol 50 ppm

β-Sitosterol (mg/ml)	Stigmasterol (mg/ml)	Lupeol (mg/ml)
4.7±0.49	3.38±0.48	1.0±0.10

Role of non polar phyto-components on PCOS rat model

1. Effect of non polar phyto-components of *Aloe vera* gel on Histology

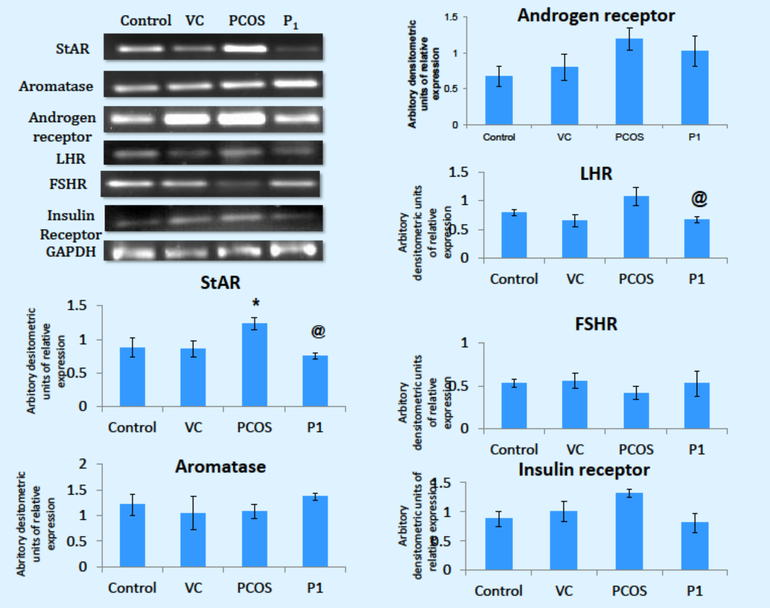


2. Effect of non polar phyto-components of *Aloe vera* gel on Hormonal profile

Groups	Testo-sterone (ng/ml)	Estradiol (ng/ml)	Prog-esterone (ng/ml)	Insulin (μIU/ml)	HOMA-IR
Control	2.6±1.1	67±2.5	14±1.5	12.3±0.6	1.8±0.1
Vehicle Control	2.4±0.2	67.3±7.6	7.9±1.2	13.5±0.76	2.5±0.2
PCOS	12±1.5**	61.3±9.6	5.5±1.2**	21±1.0**	4.5±0.3***
P_1	4.5±1.4@	72±14.5	11.5±3.5@	9.1±1.2@@@	1.4±0.1@@@

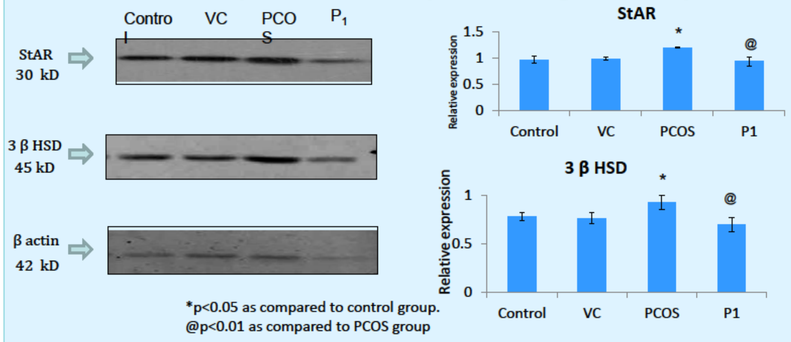
N=3,Mean±SEM,
**P<0.01; ***P<0.001 as compared to Control group.
@ p<0.05 @@@ p<0.001 as Compared to PCOS Group.

3. Effect of non polar phyto-components of *Aloe vera* gel on Transcript of key proteins of steroidogenesis



*P<0.05 as compared to Control group. @<0.05 as compared to PCOS group.

4. Effect of non polar phyto-components of *Aloe vera* gel on Protein expression of key steroidogenic enzymes



*p<0.05 as compared to control group.
@p<0.01 as compared to PCOS group

Conclusion

≈Letrozole treated rat exhibited no. of peripheral cysts in ovary, glucose intolerance, arrested cyclicity (data not shown) and altered hormonal profile which confirmed PCOS rat model.

≈Chromatographic analysis of non polar fraction of AVG suggested that it is enriched with phyto-sterols namely **sitosterol, stigmasterol, lupeol** and other minor sterols.

≈ Non polar phyto-components of *Aloe vera* helps to back to normal structure function of ovary by decreasing peripheral cysts, normalized hormonal profile and normal follicular growth.

≈ Treatment of Non polar fraction *of AVG* decreased transcripts of StAR, LH Receptor and Insulin Receptor compared to PCOS group; while other proteins-FSH Receptor, Aromatase did not show any significant change.

≈ Protein expression of StAR, 3βHSD which were altered in PCO phenotype; reverted back as similar to control values when treated with non polar fraction of *Aloe vera gel.*

≈Non polar fraction of *Aloe vera* gel has a potential to manage PCOS phenotype, by modifying steroidogenic targets. This study serve as platform for designing drugs by exploring these novel targets.

References

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❖Bhavna N. Desai, Radha H. Maharjan, Laxmipriya P. Nampoothiri. *Aloe Barbadensis* Mill. formulation restores lipid profile to normal in a letrozole-induced PCOS rat model. **Pharmacognosy Research**. **2012**; 4(2): 109-115.

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