



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم



**MONA MAGHRABY**





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# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

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**MONA MAGHRABY**





# **Efficacy and Tolerability of N-Acetyl-Cysteine for Treatment of The Early-onset Androgenetic Alopecia in Men**

Thesis

*Submitted for Fulfillment of Master's degree in  
Dermatology, Venereology & Andrology*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا نك لا علم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدق الله العظيم

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# *List of Abbreviations*

Abb.	Full term
5 $\alpha$ R.....	Five-Alpha-Reductase
AGA .....	Androgenetic alopecia
ATP .....	Adenosine triphosphate
BASP .....	Basic and specific
DHT.....	Dihydrotestosterone
FDA .....	Food and Drug Administration
FUE .....	Follicle and unit extraction
FUT .....	Follicular unit transplantation
GSH .....	Glutathione
HDAC .....	Histone-deacetylases
LLLT.....	Low-level laser therapy
NAC .....	N-acetylcysteine
PDF2 $\alpha$ .....	Prostaglandin F2 $\alpha$
PGD2.....	Prostaglandin D2
PGE2 .....	Prostaglandin E2
PRP .....	Platelet Rich Plasma
PSA.....	Prostatic specific antigen
ROS .....	Reactive oxygen species
SPSS.....	Statistical Package for Social Science
TGF- $\beta$ .....	Transforming growth factor beta
UVR .....	Ultraviolet radiation



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# 1. INTRODUCTION

Androgenetic alopecia (AGA) is a non-scarring disease with a progressive thinning of the scalp hair that follows a characteristic pattern (*Torres, 2015*). AGA, the most common form of hair loss in men, involves the progressive loss of visible pigmented terminal hair on the scalp in response to circulating androgens. AGA is an autosomal disorder which begins in puberty in genetically predisposed individuals (*Dawber, 1998*). Thinning usually begins between the age of 12 and 40 years in both sexes, and at least 50% of the men by the age of 50 and 50% of women by 60 years are more affected (*Kapadia et al., 2008*).

The pathogenesis of androgenetic alopecia involves both genetic and hormonal factors. The hair follicles are genetically targeted for androgen stimulation leading to follicular miniaturization and replacement of large pigmented hairs (terminal hairs) with shorter, thinner depigmented hairs (vellus hairs) in affected areas (*Hoffmann, 2002*). Environmental factors, the nutritional influences, metabolic syndrome, smoking and UV radiation, also play a role in the pathogenesis of AGA (*Rushton, 2002; Trueb, 2003a, b*). Recent histological studies illustrated perifollicular inflammation in the upper third of the hair follicles, suggesting that inflammation plays a pathogenic role in AGA, although clinically, AGA is considered a non-inflammatory disease (*Aslani et al., 2009; Magro et al., 2011*).



Oxidative stress and inflammation are closely linked in biological systems (*Wadley et al., 2013*). The enhanced hair loss in androgenetic alopecia was linked to several factors that increase cellular oxidative stress, including metabolic syndrome, alcohol consumption, smoking, and UV radiation (*Severi et al., 2003; Trueb, 2003a, b; Su et al., 2010; Upton et al., 2015*). AGA patients were found to suffer from oxidative stress as evidenced by the decreased total antioxidant activity as well as an increased malondialdehyde levels (*Prie et al., 2016*). *Erdogan et al. (2017)* investigated the oxidative stress in early onset androgenetic alopecia and found that the total oxidant levels and oxidative stress index are higher in younger patients with early-onset AGA.

Molecular studies of the paracrine mediators around the dermal papilla cells have shed light on the role played by reactive oxygen species (ROS) in bald scalp. Prostaglandin D2 (PGD2) was found to be elevated in the bald scalp of AGA patients and negatively affected the growth of human hair (*Geng et al., 1992; Sasaki et al., 2005*). PGD2 was found to enhance the capacity of human keratinocytes to convert the weak androgen, androstenedione, to testosterone through the involvement of ROS cellular signaling axis. The ROS scavenger, N-acetyl-cysteine, blocked the enhanced testosterone production by PGD2 (*Mantel et al., 2017*).

Transforming growth factor beta (TGF- $\beta$ ) is another key promotor of hair follicle apoptosis. TGF- $\beta$  was found to be



androgen-inducible via the induction of ROS and its induction was significantly suppressed by the ROS-scavenger, N-acetyl cysteine in the hair follicle dermal papilla cells (*Inui et al., 2003; Shin et al., 2013*).

Treatment of cases of androgenetic alopecia comprises a therapeutic challenge. AGA is neither life-threatening nor does it lead to pain; however, it leads to a significant emotional burden and is considered as a therapeutically frustrating disorder to the patients (*Cash, 2001; Khandpur et al., 2002*). The therapeutic approach to the patient with androgenetic alopecia should be global: combined treatments may obtain improvements in hair density, reduction of miniaturization and hair loss (*Rinaldi et al., 2016*). Minoxidil 2% or 5% solution is the most frequently used drug for topical application (*Abramowicz, 1998*). In men with AGA, 5% topical minoxidil was clearly superior to 2% topical minoxidil in increasing hair regrowth. Men who used 5% topical minoxidil also had an earlier response to treatment than those who used 2% topical minoxidil. Psychosocial perceptions of hair loss in men with AGA were also improved (*Elise et al., 2002*). Finasteride, a selective inhibitor of 5 $\alpha$ - reductase of type II reduces conversion of testosterone into DHT, was approved by FDA in 1997 in a dosage of 1 mg/day as a systemic therapy in adult men with mild to moderate AGA (*Abramowicz, 1998*).

N-acetylcysteine (NAC) has been widely used as an antioxidant in vivo and in vitro. NAC may act as a precursor of