



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم



**HANAA ALY**



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# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# جامعة عين شمس التوثيق الإلكتروني والميكروفيلم

## قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغييرات



## يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



**HANAA ALY**



# **Role Of Circulating Endocan as a Biomarker in Non-alcoholic Fatty Liver Disease**

A Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسبب أنك لا تعلم لنا  
إلا ما علمتنا إنك أنت  
العليم الكبير

صدقة الله العظيم

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## List of Abbreviations

Abbreviation	Full name
<b>NAFLD</b>	nonalcoholic fatty liver disease
<b>MAFLD</b>	metabolic (dysfunction) associated fatty liver disease
<b>T2DM</b>	type 2 diabetes mellitus
<b>TG</b>	triglyceride
<b>HDL</b>	high-density lipoprotein
<b>MS</b>	metabolic syndrome
<b>FFAs</b>	free fatty acids
<b>VLDLs</b>	very low density lipoproteins
<b>DNL</b>	de novo lipogenesis
<b>GLP-1</b>	Glucagon-like insulinotropic peptide-1
<b>FXR</b>	farnesoid X receptor
<b>SOD</b>	superoxide dismutase
<b>Gpx</b>	glutathione peroxidase
<b>SOD2</b>	superoxide dismutase 2
<b>PEMT</b>	phosphatidylethanolamine Nmethyltransferase
<b>FADS1</b>	fatty acid desaturase 1
<b>KLF6</b>	Kruppel-like factor 6
<b>SNP</b>	single-nucleotide polymorphism
<b>MRI</b>	magnetic resonance imaging
<b>CT</b>	computed tomography
<b>AAR</b>	alanine aminotransferase ratio
<b>HIS</b>	Hepatic Steatosis Index
<b>FLI</b>	Fatty Liver Index
<b>VAI</b>	Visceral Adiposity index
<b>PDFF</b>	proton density fat fraction
<b>MRS</b>	Magnetic resonance spectroscopy

## *List of Abbreviations*

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<b>CAP</b>	Controlled attenuation parameter
<b>HFD</b>	high-fat diet
<b>LT</b>	liver transplantation
<b>HCV</b>	hepatitis C virus
<b>US</b>	ultrasound
<b>HCC</b>	hepatocellular carcinoma

## **Introduction**

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most prevalent chronic liver disease in developed nations in recent years. It is defined as the presence of 5% steatosis in the absence of secondary causes of fat accumulation in the liver (**Arias-Loste et al., 2014**). Prevalence of NAFLD is growing, even in the developing world, because of the global obesity epidemic (**Kabbany et al., 2017**).

Moreover, very close association between the disease and metabolic syndrome has been identified (**Carr et al., 2016**). The natural history of NAFLD is not well established, with significant knowledge gaps about the marked inter-individual variations in disease onset, progression, and complications. NAFLD represents a wide spectrum of clinical entities from asymptomatic hepatic steatosis to more advanced liver disease with hepatic failure or hepatocellular carcinoma (**Rinella et al., 2015**).

The rate of disease progression in most cases is slow, although rapid development of advanced liver disease may be occasionally found. About one-third of people eventually develop NASH; however, regression of fibrosis is also noticed in about 20% of these cases. NAFLD is considered as a metabolic disorder that results from complex interaction between genetic, hormonal, and nutritional factors (**Oh et al., 2016**).

Recent evidence suggests that several genetic risk factors predispose to the development and progression of NAFLD. NAFLD remains asymptomatic in a significant proportion of patients, and the diagnosis is often suspected when liver functions are found abnormal on biochemical testing or when hepatic imaging suggest fatty liver, when performed for some other reasons (**López-Velázquez et al., 2014**).

NAFLD fibrosis score (NFS) using clinical and biochemical parameters to predict the severity of liver involvement is the most validated non-invasive tool to assess the disease. NFS is based on age, body mass index, aspartate transaminase (AST), ALT, platelets, albumin, and presence or absence of impaired fasting glucose (**Angulo et al., 2007**).

There is no single intervention that is proven to be fully effective in the treatment and cure of NAFLD. The main goals of treatment are to improve steatosis and to prevent progression of the disease. Intense lifestyle modification and treatment of the risk factors are the cornerstones of disease management. Medical and surgical interventions serve as second-line treatments, or adjuvants. As a result, there has been increased recognition of the need to assess and closely monitor individuals for risk factors of components of NAFLD and NASH, as well as the severity of these conditions using biomarkers (**Verma et al.,2013**).

Endocan, previously called endothelial cell specific molecule-1 is a novel endothelium derived soluble dermatan sulfate proteoglycan. It has the property of binding to a wide range of bioactive molecules associated with cellular signaling and adhesion and thus regulating proliferation, differentiation, migration, and adhesion of different cell types in health and disease. An increase in tissue expression or serum level of endocan reflects endothelial activation and neovascularization which are prominent pathophysiological changes associated with inflammation and tumor progression (**Kali et al.,2014**).

New insights and diagnostic improvements in NAFLD such as transient elastography and FibroScan are trending. However, focusing on noninvasive, cheap, and useful biomarkers in clinical practice is mandatory. In this way, the role of circulating biomarkers related to

endothelial dysfunction and the severity of underlying liver disease need to be investigated.

It is suggested that there is a role of endocan in vascular contribution to organ-specific inflammation and in endothelium-dependent pathological disorders including many disorders such as systemic inflammatory syndrome. Endocan is not investigated thoroughly in different stages of liver diseases, such as NAFLD (**Erman et al.,2020**).