

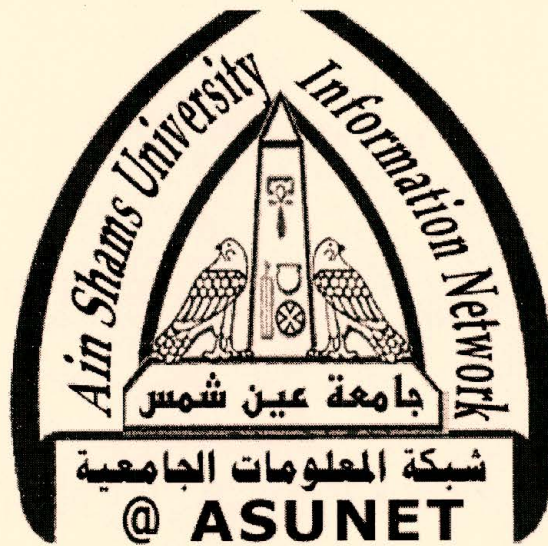


شبكة المعلومات الجامعية

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شبكة المعلومات الجامعية  
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# شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



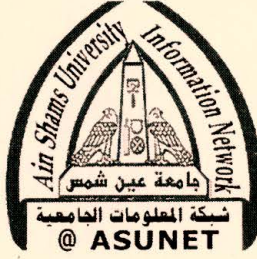
شبكة المعلومات الجامعية

# جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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## ترد بالاصل



# **Use of antisense *in vitro* for inhibition of hepatitis C virus replication**

A thesis Submitted to  
Chemistry Department  
Faculty of Science  
Cairo University

**For the degree of Master Of Science  
(in Biochemistry).**

**Submitted By**

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**Faculty of Science  
Cairo University  
2009**

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**Prof. Dr. Mostafa K. El Awady**

A handwritten signature in black ink, enclosed within a large, irregular oval shape. The signature itself consists of stylized, overlapping letters and flourishes.

## ACKNOWLEDGEMENTS

First and foremost thanks for **ALLAH**

Several outstanding individuals have contributed to making this journey unforgettable and it is to all of them that I feel deeply indebted:

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## Abstract

**Introduction:** Although interferon and ribavirin combined therapy is the only approved HCV therapy, this therapy is costly, prolonged, and is associated with significant adverse effects. Furthermore; its outcome is unfortunately poor with genotype 4. Development of alternative therapy for this genotype is of a paramount importance. Inhibitions of HCV gene expression in vitro by the use of antisense phosphorothioate oligodeoxynucleotides (S-ODN) against internal ribosome entry site (IRES) elements were associated with favorable results. **Methods:** To assess S-ODN activity, IRES domain III derived from nine Egyptian patients infected with genotype 4a were amplified, cloned and sequenced. In addition, IRES domain IV sequences that belongs to another group of patients infected with genotype 4a that were previously performed in our laboratory were obtained from GenBank. Alignment of both domains revealed that domain IV is highly conserved over loop III d which showed less sequence conservation. Such conservation suggests higher efficiency of S-ODN1 (directed against domain IV) than S-ODN2 (directed against loop III d). Effect of mismatched oligonucleotides on intracellular HCV RNA levels was also studied by using S-ODN1 altered sequence (S-ODN1\*) after random introduction of a single nucleotide substitution which showed no significant effect on S-ODN1 inhibitory effect on viral replication. The efficiency of S-ODN1 to inhibit viral replication in two different cell types was then investigated using HepG2 cells and PBMCs. **Results:** The current study have shown that SODN1 was efficiently able to inhibit viral replication in infected HepG2 cells while; in contrast, it failed to inhibit viral replication in PBMCs. **Conclusion:** The antisense oligonucleotides displayed differential inhibitory effects in different types of HCV permissible cells suggesting that S-ODN1 may inhibit HCV replication via cell specific mechanisms (pathways).

Key words:

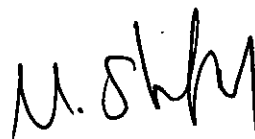
HCV, S-ODN, IRES, alignment, HepG2, PBMCs, viral replication

Supervisors

1-

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