

**COMPARATIVE STUDY OF THE  
RENOPROTECTIVE EFFECT OF ANGIOTENSIN  
CONVERTING ENZYME INHIBITORS, HYDROXY  
METHYL GLUTARAYL Co-A REDUCTASE  
INHIBITORS AND ALDOSTERONE RECEPTORS  
ANTAGONISTS ON EXPERIMENTALLY INDUCED  
NEPHROTIC SYNDROME IN ALBINO RATS**

**Thesis for partial fulfillment of  
M.D. in Medical Pharmacology**

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2013

## *Abstract*

Heavy glomerular proteinuria, also known as nephrotic syndrome, is a common feature of numerous primary and secondary nephropathies, accompanied with a high rate of recurrence (relapses) and progression to chronic kidney failure. Nevertheless, current therapy is still not fully satisfactory; this led to an arousal of some promising therapeutic strategies in which their positioning should be evidenced. *Objective:* is to demonstrate and compare the possible renoprotective effects of some proposed therapeutic strategies including the angiotensin converting enzyme inhibitors, the aldosterone receptor blockers and the lipid lowering HMG-CoA reductase enzyme inhibitors, on *adriamycin*-induced nephrotic syndrome in male albino rats. *Methodology:* 54 male albino rats were divided in 9 groups, in which **Group I** was the control group receiving a single saline injection followed 2 weeks later by daily oral saline therapy for 2 weeks, groups (II-IX) received single *adriamycin* injection (5 mg/kg) to induce nephrotic syndrome followed 2 weeks later by daily therapy for 2 weeks, **group II (nephrotic, non-treated rats):** received daily *oral saline* (2.5 ml /kg), **group III (nephrotic rats, captopril treated):** received daily *oral Captopril* (50 mg/kg), **group IV (nephrotic rats, spironolactone treated):** received daily *oral spironolactone* (25 mg/kg), **group V (nephrotic rats, simvastatin treated):** received daily *oral simvastatin* (10 mg/kg), **group VI (nephrotic rats, captopril and spironolactone treated), group VII (nephrotic rats, captopril and simvastatin treated), group VIII (nephrotic rats, spironolactone and simvastatin treated) and group IX (nephrotic rats; captopril, spironolactone and simvastatin treated).** *Results:* revealed reduction in proteinuria and triglycerides levels following captopril and spironolactone administration either given separately, as double therapy or as triple therapy when added to statin. However, statin therapy revealed an eminent effect on serum lipid levels and endothelial dysfunction when administered as monotherapy, double therapy with either drugs or as triple therapy. *Conclusion:* Angiotensin converting enzyme inhibitors and aldosterone receptor blockers represent promising alternative strategies to reduce proteinuria and, possibly, delay progression of renal disease. This renoprotective effect increased with their combination as double therapy or as triple therapy when added to statin. However, the effect of statin therapy was more evident in improving significant endothelial dysfunction.

*Key words:* nephrotic syndrome, renoprotection, captopril, spironolactone, statin.

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## *Acknowledgement*

*First and foremost thanks are to God the most kind and the most merciful,  
“who taught man what he did not know”.*

*I would like to express my appreciation and sincere gratitude to Prof. Dr. / **Samia El-Halawany**, professor of pharmacology, faculty of Medicine, Cairo University, for her eminent supervision, valuable guidance and patience that made her meticulously revise this work word by word.*

*There is no word capable of expressing my gratitude and appreciation to Prof. Dr. / **Mohsen Sami Selim**, professor of pharmacology, faculty of Medicine, Cairo University, for resolving the most difficult obstacles I met throughout this work. I shall never forget his excellent guidance, continuous encouragement and most valuable suggestions.*

*I would like to express my deep appreciation and gratitude to Prof. Dr. / **Olfat Gamil Shaker**, professor of medical biochemistry, faculty of Medicine, Cairo University, for her generous assistance and great effort in helping me to investigate the blood and urine samples that I have taken in this study.*

*I will always be grateful to Dr. / **Ahmed Abd El-Rahman**, lecturer of pharmacology, faculty of Medicine, Cairo University, for his kind guidance, supervision and valuable instructions.*

*My special appreciation and thanks go to Dr. / **Hossam Hussein**, assistant professor of pathology, faculty of Medicine, Cairo University, who devoted much of his time and a remarkable effort in helping me to comment on the histopathological examination of the samples collected in this work.*

*I would like to express my appreciation to **Dr./Omayma Hamed Abou el Ela**, Professor of Forensic and Toxicology, faculty of Medicine, Cairo University, for her meticulous effort in the statistical analysis.*

*I would like to thank **Dr./ Hesham Mohamed Mahmoud**, assistant professor of pharmacology, faculty of Medicine, Cairo University, and shall never forget his excellent guidance, continuous encouragement and most valuable suggestions.*

## Contents

<i>Item</i>	<i>Page</i>
<b>Introduction and Aim of work</b> .....	<b>1</b>
<b>Review of Literature</b> .....	<b>6</b>
<b>Material and Methods</b> .....	<b>29</b>
<b>Results</b> .....	<b>35</b>
<b>Discussion</b> .....	<b>114</b>
<b>Conclusion</b> .....	<b>143</b>
<b>Summary</b> .....	<b>144</b>
<b>References</b> .....	<b>149</b>
<b>Arabic Summary</b> .....	<b>188</b>

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### **List of Abbreviations**

- **ACEIs** : angiotensin-converting enzyme inhibitors
- **ACTH** : Adrenocorticotrophic hormone
- **ADR** : adverse drug reaction
- **AIDS** : acquired immunodeficiency syndrome.
- **ANP** : Atrial natriuretic peptide
- **ARBs**: angiotensin receptor blockers
- **AT1R** : angiotensin type 1 receptor
- **AT-II** : Angiotensin II
- **C** : Captopril
- **CSA** : cyclosporin A
- **CYP** : cyclophosphamide
- **ESKD** : end-stage kidney disease
- **FSGS** : focal segmental glomerulosclerosis
- **HMG-CoA**: hydroxymethyl-glutaryl Co-enzyme A
- **Hx & Eu**: Haematoxylin and Eosin
- **Ig**: immunoglobulin
- **IMN** : Idiopathic membranous nephropathy
- **INS** : idiopathic nephrotic syndrome
- **MCNS** : minimal change nephrotic syndrome
- **MN**: membranous nephropathy
- **NS** : Nephrotic syndrome
- **PE**: pulmonary embolism
- **PHN** : passive Heymann nephritis
- **PNS** : Primary nephrotic syndrome
- **PV** : plasma volume
- **RAAS** : renin-angiotensin-aldosterone system
- **RENaC** : renal epithelial sodium channel
- **Sm** : Simvastatin
- **Sp** : Spironolactone
- **SRNS** : steroid resistant NS
- **SSNS** : steroid-sensitive NS
- **TAC** : tacrolimus
- **TEC**: thromboembolic complications

## List of tables

Table No. / Title	Page
<b>Table (1):</b> -----	<b>39</b>
Effect of oral <i>Captopril</i> (C) “50 mg/kg/day”, <i>Spironolactone</i> (Sp) “25 mg/kg/day” and <i>Simvastatin</i> (Sm) “10 mg/kg/day” for 2weeks on the urinalysis of male albino rats with I.V. <i>adriamycin</i> (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS”.	
<b>Table (2):</b> -----	<b>40</b>
% changes in the mean urinalysis values produced by oral <i>Captopril</i> (C) “50 mg/kg/d”, <i>Spironolactone</i> (Sp) “25 mg/kg/day”, <i>Simvastatin</i> (Sm) “10 mg/kg/day” and their combination for 2weeks in the male albino rats with I.V. <i>adriamycin</i> (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to normal group-I and non-treated group-II	
<b>Table (3):</b> -----	<b>41</b>
% changes in the mean urinalysis values produced by oral <i>Captopril</i> (C) “50 mg/kg/day” combination with <i>Spironolactone</i> (Sp) “25 mg/kg/day” and/or <i>Simvastatin</i> (Sm) “10 mg/kg/day” for 2weeks in male albino rats with I.V. <i>adriamycin</i> (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to <i>Captopril</i> alone in group-III.	
<b>Table (4):</b> -----	<b>42</b>
% changes in the mean urinalysis values produced by oral <i>Spironolactone</i> (Sp) “25 mg/kg/day” combination with <i>Captopril</i> (C) “50 mg/kg/day” and/or <i>Simvastatin</i> (Sm) “10 mg/kg/day” for 2weeks in male albino rats with I.V. <i>adriamycin</i> (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to <i>Spironolactone</i> alone in group-IV.	
<b>Table (5):</b> -----	<b>43</b>
% changes in the mean urinalysis values produced by oral <i>Simvastatin</i> (Sm) “10 mg/kg/day” combination with <i>Captopril</i> (C) “50 mg/kg/day” and/or <i>Spironolactone</i> (Sp) “25 mg/kg/day” for 2weeks in male albino rats with I.V. <i>adriamycin</i> (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to <i>Simvastatin</i> alone in group-V.	
<b>Table (6):</b> -----	<b>63-64</b>
Effect of oral <i>Captopril</i> (C) “50 mg/kg/d”, <i>Spironolactone</i> (Sp) “25 mg/kg/day” and <i>Simvastatin</i> (Sm) “10 mg/kg/day” for 2weeks on the mean serum biochemical parameters of male albino rats with I.V. <i>adriamycin</i> (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS”	

**Table (7): ----- 65**

% changes in the mean serum biochemical parameters produced by oral Captopril (C) “50 mg/kg/day”, Spironolactone (Sp) “25 mg/kg/day”, Simvastatin (Sm) “10 mg/kg/day” and their combination for 2weeks in male albino rats with I.V. adriamycin (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to normal group-I and non-treated group-II

**Table (8): ----- 66**

% changes in the mean serum biochemical parameters produced by oral Captopril (C) “50 mg/kg/day” combination with Spironolactone (Sp) “25 mg/kg/day” and/or Simvastatin (Sm) “10 mg/kg/day” for 2weeks in male albino rats with I.V. adriamycin (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to Captopril alone in group-III

**Table (9): ----- 67**

% changes in the mean *serum* biochemical parameters produced by oral *Spironolactone* (Sp) “25 mg/kg/day” combination with *Captopril* (C) “50 mg/kg/day” and/or *Simvastatin* (Sm) “10 mg/kg/day” for 2weeks in male albino rats with I.V. *adriamycin* (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to *Spironolactone* alone in group-IV.

**Table (10): ----- 68**

% changes in the mean serum biochemical parameters produced by oral Simvastatin (Sm) “10 mg/kg/day” combination with Captopril (C) “50 mg/kg/day” and/or Spironolactone (Sp) “25 mg/kg/day” for 2weeks in male albino rats with I.V. adriamycin (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to Simvastatin alone in group-V

**Table (11): ----- 88**

Effect of oral *Captopril* (C) “50 mg/kg/day”, *Spironolactone* (Sp) “25 mg/kg/day” and *Simvastatin* (Sm) “10 mg/kg/day” for 2weeks on the mean dose of acetylcholine needed to produce 50% reduction of noradrenaline induced contraction in the isolated aortic rings of male albino rats with I.V. *adriamycin* (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS”.

**Table (12): ----- 89**

% Changes in the mean dose of acetylcholine needed to produce 50% reduction of noradrenaline induced submaximal contraction in the isolated aortic rings of male albino rats with I.V. adriamycin (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” treated with oral Captopril (C) “50 mg/kg/day”, Spironolactone (Sp) “25 mg/kg/day”, Simvastatin (Sm) “10 mg/kg/day” and their combination for 2weeks.

**Table (13): ----- 90**

% changes in the mean dose of acetylcholine needed to produce 50% reduction of noradrenaline induced sub-maximal contraction in the isolated aortic rings of male albino rats by oral *Captopril* (C) “50 mg/kg/day” combination with *Spironolactone* (Sp) “25 mg/kg/day” and/or *Simvastatin* (Sm) “10 mg/kg/day” for 2weeks in male albino rats with I.V. *adriamycin* (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS” compared to group-III, IV and V.

**Table (14): ----- 104**

Effect of oral *Captopril* (C) “50 mg/kg/day”, *Spironolactone* (Sp) “25 mg/kg/day”, *Simvastatin* (Sm) “10 mg/kg/day” and their combinations for 2weeks on the mean kidneys weight of male albino rats with I.V. *adriamycin* (Ad) “5mg/kg single dose” induced nephrotic syndrome “NS”.

**Table (15): ----- 107**

Effect of oral *Captopril* (C) “50 mg/kg/day”, *Spironolactone* (Sp) “25 mg/kg/day”, *Simvastatin* (Sm) “10 mg/kg/day” and their combinations for 2weeks on the mean histopathological glomerulosclerosis score of male albino rats with I.V. *adriamycin* (Ad) “5mg/kg single dose” induced nephrotic syndrome.

\*\*\*\*\*

### List of diagrams

Diagram No.	Page
diagram-1	8
diagram-2	9
diagram-3	9

\*\*\*\*\*



## List of Figures

Figure number/ Title	Page No.
<b><u>Fig. (1):</u></b> Effect of IV adriamycin (Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS) on the urine volume of male albino rats in groups GII-IX compared to normal rats in G-I	<b>44</b>
<b><u>Fig. (2):</u></b> Effect of IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS) on the microalbuminuria of male albino rats in groups GII-IX compared to normal rats in G-I	<b>45</b>
<b><u>Fig. (3):</u></b> Effect of IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS) on the urine creatinine of male albino rats in groups GII-IX compared to normal rats in G-I	<b>46</b>
<b><u>Fig. (4):</u></b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on urine volume of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>47</b>
<b><u>Fig. (5):</u></b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on microalbuminuria of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>48</b>
<b><u>Fig. (6):</u></b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on urine creatinine of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>49</b>
<b><u>Fig. (7):</u></b> % changes in the mean urine volume produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose’ induced nephrotic syndrome(NS) compared to normal group-I and non treated group-II.	<b>50</b>

Figure number/ Title	Page No.
<b>Fig. (8):</b> % changes in the mean microalbuminuria produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose' induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II.	<b>51</b>
<b>Fig. (9):</b> % changes in the mean urine creatinine produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose' induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II.	<b>52</b>
<b>Fig. (10):</b> % changes in the mean urinalysis values produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose induced nephrotic syndrome (NS) compared to Captopril alone in group-III	<b>53</b>
<b>Fig. (11):</b> % changes in the mean urinalysis values produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose induced nephrotic syndrome (NS) compared to Spironolactone alone in group-IV	<b>54</b>
<b>Fig. (12):</b> % changes in the mean urinalysis values produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose induced nephrotic syndrome (NS) compared to Simvastatin alone in group-V	<b>55</b>
<b>Fig. (13):</b> Effect of IV adriamycin(Ad)'5mg/kg single dose' induced nephrotic syndrome (NS) on the mean serum total protein of male albino rats in groups GII-IX compared to normal rats in G-I	<b>69</b>
<b>Fig. (14):</b> Effect of IV adriamycin(Ad) '5mg/kg single dose' induced	<b>70</b>

Figure number/ Title	Page No.
nephrotic syndrome (NS) on the mean serum cholesterol of male albino rats in groups GII-IX compared to normal rats in G-I	
<b>Fig. (15):</b> Effect of IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS) on the mean serum triglycerides of male albino rats in groups GII-IX compared to normal rats in G-I	<b>71</b>
<b>Fig. (16):</b> Effect of IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS) on the mean serum urea of male albino rats in groups GII-IX compared to normal rats in G-I	<b>72</b>
<b>Fig. (17):</b> Effect of IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS) on the mean serum creatinine of male albino rats in groups GII-IX compared to normal rats in G-I	<b>73</b>
<b>Fig. (18):</b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean serum total protein of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>74</b>
<b>Fig. (19):</b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean serum cholesterol of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>75</b>
<b>Fig. (20):</b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean serum triglycerides of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>76</b>
<b>Fig. (21):</b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean serum urea of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>77</b>

Figure number/ Title	Page No.
<b>Fig. (22):</b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean serum creatinine of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>78</b>
<b>Fig. (23):</b> % changes in the mean serum total protein produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose’ induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II	<b>79</b>
<b>Fig. (24):</b> % changes in the mean serum cholesterol produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose’ induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II	<b>80</b>
<b>Fig. (25):</b> % changes in the mean serum triglycerides produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose’ induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II	<b>81</b>
<b>Fig. (26):</b> % changes in the mean serum urea produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose’ induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II	<b>82</b>
<b>Fig. (27):</b> % changes in the mean serum creatinine produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose’ induced nephrotic syndrome (NS) compared to normal group-I and non treated group-II	<b>83</b>

<b>Figure number/ Title</b>	<b>Page No.</b>
<b><u>Fig. (28):</u></b> changes in the mean serum biochemical parameters produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose induced nephrotic syndrome (NS) compared to Captopril alone in group-III	<b>84</b>
<b><u>Fig. (29):</u></b> % changes in the mean serum biochemical parameters produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose induced nephrotic syndrome (NS) compared to Spironolactone alone in group-IV	<b>85</b>
<b><u>Fig. (30):</u></b> % changes in the mean serum biochemical parameters produced by oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks in the male albino rats with IV adriamycin (Ad) 5mg/kg single dose induced nephrotic syndrome (NS) compared to Simvastatin alone in group-V	<b>86</b>
<b><u>Fig. (31):</u></b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean acetylcholine dose needed to produce 50% reduction of noradrenaline induced submaximal contraction of the isolated aortic rings of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>91</b>
<b><u>Fig. (32):</u></b> % changes in the mean acetylcholine dose needed to produce 50% reduction of noradrenaline induced submaximal contraction of the isolated aortic rings of male albino rats treated with oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks compared to normal group-I and non treated group-II	<b>92</b>

Figure number/ Title	Page No.
<b>Fig. (33):</b> % changes in the mean dose of acetylcholine needed to produce 50% reduction of noradrenaline induced submaximal contraction of the isolated aortic rings of male albino rats with IV adriamycin (Ad) 5mg/kg single dose' induced nephrotic syndrome (NS) treated with oral Captopril (C) 50mg/kg/day, spironolactone (Sp) 25mg/kg/day, simvastatin (Sm) 10mg/kg/day and their combination for 2 weeks, compared to (C), (Sp) and (Sm) treated groups-III, IV and V, respectively.	<b>93</b>
<b>Fig. (34):</b> Effect of oral Captopril(C) '50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the mean kidneys weight of male albino rats with IV adriamycin (Ad) 5mg/kg single dose' induced nephrotic syndrome (NS)	<b>104</b>
<b>Fig. (35):</b> High power magnification for a glomerulus with normal lobular capsular pattern "i.e. injury score 0", capillary tuft and no adhesion for a normal control group-I.	<b>108</b>
<b>Fig. (36):</b> High power magnification for a glomerulus with 100% sclerosis (i.e. injury score 4+ "ticked by black arrows"); for a male rat of non-treated group-II that received oral <i>Saline</i> for 2weeks on top of I.V. <i>adriamycin</i> "5mg/kg single dose" induced nephrotic syndrome. There was evidence of mild tubular dilatation which predominantly affected the juxtamedullary tubules. Focal areas of interstitial fibrosis were observed surrounding some of the dilated tubules.	<b>108</b>
<b>Fig. (37):</b> High power magnification for a glomerulus with 50% sclerosis (i.e. injury score 2+ "ticked by black arrows") and no adhesion; for a male rat of group-III that received oral mono-therapy <i>Captopril</i> "50 mg/kg/day" for 2weeks on top of I.V. <i>adriamycin</i> "5mg/kg single dose" induced nephrotic syndrome.	<b>109</b>
<b>Fig. (38):</b> High power magnification for a glomerulus with 50% sclerosis (i.e. injury score 2+ "ticked by black arrows") and no adhesion; for a male rat of group-IV that received oral mono-therapy <i>Simvastatin</i> "10 mg/kg/day" for 2weeks on top of I.V. <i>adriamycin</i> "5mg/kg single dose" induced nephrotic syndrome.	<b>109</b>

Figure number/ Title	Page No.
<b>Fig. (39):</b> High power magnification for a glomerulus with 100% sclerosis (i.e. injury score 4+ “ticked by black arrows”) for a male rat of group- <b>V</b> that received oral mono therapy <i>Simvastatin</i> “10 mg/kg/day” for 2weeks on top of I.V. <i>adriamycin</i> “5mg/kg single dose” induced nephrotic syndrome. There was evidence of mild tubular dilatation which predominantly affected the juxtamedullary tubules. Focal areas of interstitial fibrosis were observed surrounding some of the dilated tubules	<b>110</b>
<b>Fig. (40):</b> High power magnification for a glomerulus with 25% sclerosis (i.e. injury score 1+ “ticked by black arrows”) and no adhesion; for a male rat of group- <b>VI</b> that received oral double therapy <i>Captopril</i> “50 mg/kg/day” and <i>Spironolactone</i> “25 mg/kg/day” for 2weeks on top of I.V. <i>adriamycin</i> “5mg/kg single dose” induced nephrotic syndrome	<b>110</b>
<b>Fig. (41):</b> High power magnification for a glomerulus with 25% sclerosis (i.e. injury score 1+ “ticked by black arrows”) and no adhesion; for a male rat of group- <b>VII</b> that received oral double therapy <i>Captopril</i> “50 mg/kg/day” and <i>Simvastatin</i> “10 mg/kg/day” for 2weeks on top of I.V. <i>adriamycin</i> “5mg/kg single dose” induced nephrotic syndrome.	<b>111</b>
<b>Fig. (42):</b> High power magnification for a glomerulus with 75% sclerosis (i.e. injury score 3+ “ticked by black arrows”) and no adhesion; for a male rat of group- <b>VIII</b> that received oral double therapy <i>Spironolactone</i> “25 mg/kg/day” and <i>Simvastatin</i> “10 mg/kg/day” for 2weeks on top of I.V. <i>adriamycin</i> “5mg/kg single dose” induced nephrotic syndrome.	<b>111</b>
<b>Fig. (43):</b> High power magnification for a glomerulus with 25% sclerosis (i.e. injury score 1+ “ticked by black arrows”) and no adhesion for a male rat of group- <b>IX</b> that received oral triple therapy <i>Captopril</i> “50 mg/kg/day”, <i>Spironolactone</i> “25 mg/kg/day” and <i>Simvastatin</i> “10 mg/kg/day” for 2weeks on top of I.V. <i>adriamycin</i> “5mg/kg single dose” induced (NS)	<b>112</b>
<b>Fig. (44):</b> Effect of oral Captopril(C) ‘50mg/kg/day, spironolactone(Sp) 25mg/kg/day, simvastatin(Sm) 10mg/kg/day and their combination for 2 weeks on the glomerulosclerosis of male albino rats with IV adriamycin(Ad) ‘5mg/kg single dose’ induced nephrotic syndrome (NS)	<b>113</b>