Beneficial effects of melatonin and alpha lipoic acid on lopinavir/ritonavir-induced alterations in serum lipid and glucose levels of male albino rats

Elias Adikwu*, Brambaifa Nelson, Wolfe Atuboyedia Obianime

Department of Pharmacology, Faculty of Basic Medical Sciences, University of Port Harcourt, Choba, Rivers State Nigeria

Received: January 2016; Accepted: March 2016

Abstract

The use of lopinavir/ritonavir (LPV/r) has been associated with alterations in serum lipid and glucose levels. This study was designed to investigate the effects of melatonin (MT) and alpha lipoic acid (ALA) on LPV/r-induced changes in serum levels of triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and glucose (GL) levels in male albino rats. Rats in group A1 (placebo control) and group A2 (solvent control) were orally treated with normal saline and 1% ethanol respectively. Groups B-F contained 15 rats each which were divided into 3 groups of 5 rats each. Rats in group B were orally treated with MT (10 mg kg⁻¹/day), ALA (10 mg kg⁻¹/day) and a combination of MT and ALA, accordingly. Rats in group C were orally treated with 22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day of LPV/r, accordingly. Rats in groups D-F were orally treated with MT (10 mg kg⁻¹/day), ALA (10 mg kg⁻¹/day) and combined doses of ALA and MT before oral treatment with 22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day of LPV/r, accordingly. All rats were treated for 30 days and at the end of the drug treatment, the serum levels of lipid fractions and glucose were evaluated. Treatment with MT and ALA significantly (p<0.05) decreased baseline serum levels of TG, TC, VLDL-C, LDL-C and GL, but these parameters were significantly (p<0.05) increased in a dose-dependent manner in LPV/r-treated rats when compared to placebo control. Administration of MT and ALA prior to treatment with LPV/r significantly (p<0.05) decreased serum levels of TG, TC, VLDL-C, LDL-C and GL when compared to LPV/r-treated rats. However, decreases obtained in rats pretreated with combined doses of MT and ALA were significantly (p<0.05) different when compared to their individual doses. This study showed that MT and ALA can serve as remedies for LPV/r-induced alterations in serum lipid and glucose levels.

Key words: lopinavir/ritonavir, melatonin, alpha lipoic acid, lipid, glucose, rats

Introduction

Highly active antiretroviral therapy (HAART) involves a combination of three or four classes of antiretroviral drugs. The combination may include two nucleoside analogue reverse transcriptase inhibitors (NRTIs) and one or two protease inhibitors (PIs), or non-nucleoside reverse transcriptase inhibitors (NNRTIs) and cell membrane fusion inhibitors (BHIVA, 2014; Lenhard et al., 2000). The use of HAART has improved survival among people living with human immunodeficiency virus (HIV) with significant decrease in morbidity and mortality due to HIV (Wynn et al., 2004). However, the uses of antiretroviral drugs have been associated with alterations in plasma lipid and glucose levels, which could precipitate adverse cardiovascular events (Grunfeld et al., 2010; Haubrich et al., 2009).
Among the classes of antiretroviral drugs, alterations in plasma lipids and glucose levels are frequent class-related adverse effects of protease inhibitors which could limit their uses, especially in patients with pre-existing cardiovascular risk. Among the protease inhibitors, higher and frequent incidence of alterations in plasma lipid and glucose levels may be common with the use of lopinavir/ritonavir (LPV/r) (Eron et al., 2006; Hill et al., 2009). Studies have shown that alterations in plasma lipids with LPV/r therapy could be characterized primarily by two factors: elevated plasma triglycerides (TG), and decreased HDL-cholesterol (HDL-C). Also, increases in total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) were frequently observed with LPV/r use (Mulligan et al., 2008). Alterations in serum glucose (GL) and lipid levels could involve oxidative stress. In addition, higher serum levels of malondialdehyde have been reported in subjects with hyperlipidemia (Minhajuddin et al., 2005).

Melatonin (MT) is an indoleamine hormone secreted by the pineal gland of all mammals which is under the control of the central nervous system via the suprachiasmatic nucleus (SCN) of the hypothalamus (Altun et al., 2002). It is a lipophilic and hydrophilic antioxidant with anti-inflammatory properties. It inhibits oxidative stress by directly scavenging and neutralizing free radicals and stimulating the activities of other antioxidants (Tan et al., 2011). It influences a variety of biological processes including circadian rhythms, neuroendocrine, cardiovascular and immune functions, as well as thermoregulation (Peschke, 2008). Studies have shown that biological effects of MT also include regulation of insulin secretion and glucose/lipid metabolism (Peschke and Muhlbaier, 2010). MT treatment was observed to markedly improved insulin sensitivity and glucose tolerance in mice on a high-fat diet (Sartoretti et al., 2009). It increased hepatic glycogen and improved liver steatosis in high-fat diet-induced diabetic mice (Shieh et al., 2011). Also, it reduced serum TC, LDL-C levels and remarkably increased HDL-C level in high fat diet-induced hyperlipidemia (Hoyos et al., 2000; Nishida et al., 2002).

Alpha lipoic acid (ALA) is a cofactor of α-ketoacid dehydrogenase complexes which has antioxidant, anti-inflammatory and immunomodulatory properties and plays a fundamental role in metabolism. ALA and its metabolite (dihydrolipoic acid) are amphiphilic molecules that can inhibit oxidative stress by scavenging free radicals in hydrophilic and lipophilic environments and can stimulate the activities of other antioxidants (Wada et al., 1997). It has been found to affect cellular metabolic processes, alter redox status of cells, and interact with thiols and other antioxidants. It is an essential cofactor of mitochondrial respiratory enzymes, including the pyruvate dehydrogenase (PDH) complex with beneficial effects on energy production (Parker et al., 2001). ALA was reported to regulate lipid and glucose metabolism with decrease in insulin resistance in rats fed with a high fat diet (See et al., 2012). It ameliorated streptozotocin-induced alterations in lipid, glucose and insulin levels and oxidative stress indices in rats (Morakinyo et al., 2013). Due to the regulatory effects of MT and ALA on lipid and glucose metabolism, this study investigated the effects of pretreatments with MT and ALA on baseline and LPV/r-induced serum levels of TG, TC, LDL-C, VLDL-C and GL levels in male albino rats.

Materials and methods

Animals

Eighty-five male albino rats used for this study were obtained from the animal house of the University of Port Harcourt, Choba, Rivers State. The rats were housed in individual cages at 21 ± 2 °C, 40–60% relative humidity and exposed to a 12-h light–dark cycle, with the light cycle coinciding with daylight hours. The rats were allowed free access to food and water ad libitum.

Drugs

LPV/r used for this study was manufactured by Myland Laboratories Limited India. The pure samples of MT and ALA were supplied by Shijiazhuang AO Pharm Import and Export Co Ltd China. All other chemicals used for this study were of analytical grade.

Dose selection

LPV/r (22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day) which represent 2, 4 and 8 times the clinical dose (Hullet al., 2009), MT (10 mg kg⁻¹/day) and ALA (10 mg kg⁻¹/day) were used for this study (Ali, 2013; Bilginoğlu et al., 2014). LPV/r was dissolved in 1% ethanol; ALA was dissolved in water while MT was dissolved in 1% ethanol and diluted with normal saline (Reyskens et al., 2013; Shagirtha et al., 2011).

Experimental design

Grouping of animals: Rats were divided into six groups A-F. Group A which served as the control contained 10 rats which were sub-divided into two groups: A1 and A2 of 5 animals each. Groups B-F, containing 15 rats each, were sub-divided into 3 groups of 5 animals each.

Control groups

Rats in group A1 (placebo control) and group A2 (solvent control) were orally treated with 0.2 ml of normal saline and 1% ethanol respectively.

Antioxidants treated groups

Rats in group B1-B3 were orally treated with 10 mg kg⁻¹/day of MT, 10 mg kg⁻¹/day of ALA, and combined doses of MT and ALA for 30 days.
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Lopinavir/ritonavir treated groups

Rats in groups C1-C3 were orally treated with 22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day of LPV/r for 30 days respectively.

Lopinavir/ritonavir and antioxidants treated groups

Rats in groups D1-D3 were orally administered with 10 mg kg⁻¹/day of MT prior to oral treatment with 22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day of LPV/r for 30 days respectively.

Rats in groups E1-E3 were orally administered with 10 mg kg⁻¹/day of ALA, prior to oral treatment with 22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day of LPV/r for 30 days respectively.

Rats in groups F1-F3 were orally administered with combined doses of MT and ALA prior to oral treatment with 22.9/5.71, 45.6/11.4 and 91.4/22.9 mg kg⁻¹/day of LPV/r for 30 days respectively.

Collection of samples

Rats were sacrificed using diethyl ether after day 30 days of treatment. Blood samples were collected via cardiac puncture and transferred into sterile sample containers. The blood samples were allowed to clot, centrifuged at 1200 rpm for 15 min and serum was extracted and evaluated for lipid profile.

Evaluation of serum lipid and glucose levels

Serum TG, TC, LDL-C and VLDL-C levels were evaluated as reported by Afolabi et al. (2012). Blood glucose level was evaluated with the aid of one touch basic meter (Lifescan, Inc., 2001 Milpitas, CA 95035, USA) (Tende et al., 2011).

Statistical analysis

Statistical analysis was performed using Graph pad prism 5 statistical package and ANOVA for comparison of the mean of the various groups. Results are expressed as mean ± standard error of mean (S.E.M). Statistical significance was set at p<0.05.

Results

Treatment with individual doses of MT and ALA insignificantly (p<0.05) decreased baseline serum levels of TC, TG, LDL-C, VDL-C and GL when compared to control. Pronounced and significant (p<0.05) decreases in TC, TG, LDL-C, VDL-C and GL when compared to control were obtained in rats treated with a combination of MT and ALA when compared to control (Table 1). On the contrary, treatment with 22.9/5.71-91.4/22.9 mg kg⁻¹/day of LPV/r significantly (p<0.05) and in a dose-dependent manner increased serum levels of TC, TG, LDL-C, VDL-C and GL when compared to control. This study obtained maximum increases in the serum levels of TC, TG, LDL-C, VDL-C and GL to 137.3 ± 4.85, 120.3 ± 5.62, 56.88 ± 3.01, 43.88 ± 3.03 and 110.25 ± 5.35 mg/dl respectively in rats treated with 91.4/22.9 mg kg⁻¹/day of LPV/r for 30 days (Tables 2-6). Interestingly, pretreatments with individual doses of MT and ALA prior to treatment with 22.9/5.71-91.4/22.9 mg kg⁻¹/day of LPV/r decreased serum levels of TC, TG, LDL-C, VDL-C and GL when compared to serum values obtained in LPV/r treated rats. Most pronounced decreases in the serum levels of TC, TG, LDL-C, VDL-C and GL were obtained in rats pretreated with a combination of ALA and MT. Serum values obtained with pretreatment using combined doses of MT and ALA were significantly (p<0.05) different when compared to serum values obtained with pretreatment using individual doses of MT and ALA (Tables 2-6).

Discussion

The uses of antiretroviral drugs have efficiently suppressed human immunodeficiency virus (HIV) replication, but long-term uses could be associated with alterations in serum lipid and glucose levels. These alterations are major risk factors for the development of cardiovascular diseases and are common among protease inhibitors. Studies have shown that increased TC and TG levels are independent risk factors that can accelerate the development of atherosclerosis and progression of atherosclerotic lesions (Estrada and Portilla, 2011). This study investigated the effects

Table 1. Effects of treatments with MT and ALA on baseline serum lipid and glucose levels of male albino rats

<table>
<thead>
<tr>
<th>Dose</th>
<th>Serum lipid and glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TG</td>
</tr>
<tr>
<td>Control (placebo)</td>
<td>45.33 ± 2.35</td>
</tr>
<tr>
<td>MT (10 mg/kg)</td>
<td>44.15 ± 3.00</td>
</tr>
<tr>
<td>ALA (10 mg/kg)</td>
<td>43.10 ± 3.22</td>
</tr>
<tr>
<td>MT+ALA</td>
<td>35.95 ± 1.21*</td>
</tr>
</tbody>
</table>

MT= Melatonin ALA= Alphalipoic acid. Results are expressed as mean ± S.E.M.

* Significant (p<0.05) difference when compared to control

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Table 2. Effects of MT and ALA on lopinavir/ritonavir-induced serum level of triglycerides in male albino rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>LPV/r</th>
<th>MT+LPV/r</th>
<th>ALA+LPV/r</th>
<th>MT+ALA+LPV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>45.33 ± 4.35</td>
<td>45.33 ± 4.35</td>
<td>45.33 ± 4.35</td>
<td>45.33 ± 4.35</td>
</tr>
<tr>
<td>22.9/5.71</td>
<td>63.45 ± 3.65</td>
<td>46.18 ± 2.86*</td>
<td>48.95 ± 1.03*</td>
<td>35.88 ± 2.67**</td>
</tr>
<tr>
<td>45.6/11.4</td>
<td>82.53 ± 4.88</td>
<td>48.13 ± 2.16*</td>
<td>50.00 ± 3.78*</td>
<td>38.33 ± 1.50**</td>
</tr>
<tr>
<td>91.4/22.9</td>
<td>120.3 ± 5.62</td>
<td>70.40 ± 3.71*</td>
<td>71.45 ± 5.08*</td>
<td>40.35 ± 3.50**</td>
</tr>
</tbody>
</table>

LPV/r = Lopinavir/ritonavir, MT = Melatonin, ALA = Alphalipoic acid. Results are expressed as mean ± S.E.M.  
*Significant (p<0.05) difference when compared to treatment with LPV/r  
** Significant (p<0.05) difference when compared to pretreatments with individual doses of MT and ALA

Table 3. Effects of MT and ALA on lopinavir/ritonavir-induced serum level of total cholesterol in male albino rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>LPV/r</th>
<th>MT+LPV/r</th>
<th>ALA+LPV/r</th>
<th>MT+ALA+LPV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>66.55 ± 3.74</td>
<td>66.55 ± 3.74</td>
<td>66.55 ± 3.74</td>
<td>66.55 ± 3.74</td>
</tr>
<tr>
<td>22.9/5.71</td>
<td>98.75 ± 4.70</td>
<td>65.68 ± 3.05*</td>
<td>68.68 ± 4.42*</td>
<td>50.20 ± 3.78**</td>
</tr>
<tr>
<td>45.6/11.4</td>
<td>123.0 ± 5.04</td>
<td>70.30 ± 4.37*</td>
<td>74.5 ± 5.19*</td>
<td>55.20 ± 2.17**</td>
</tr>
<tr>
<td>91.4/22.9</td>
<td>137.3 ± 4.85</td>
<td>80.02 ± 4.47*</td>
<td>85.5 ± 2.70*</td>
<td>57.55 ± 3.07**</td>
</tr>
</tbody>
</table>

LPV/r = Lopinavir/ritonavir, MT = Melatonin, ALA = Alphalipoic acid. Results are expressed as mean ± S.E.M.  
*Significant (p<0.05) difference when compared to treatment with LPV/r  
** Significant (p<0.05) difference when compared to pretreatments with individual doses of MT and ALA

Table 4. Effects of MT and ALA on lopinavir/ritonavir-induced serum level of low density lipoprotein cholesterol in male albino rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>LPV/r</th>
<th>MT+LPV/r</th>
<th>ALA+LPV/r</th>
<th>MT+ALA+LPV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16.20 ± 0.65</td>
<td>16.20 ± 0.65</td>
<td>16.20 ± 0.65</td>
<td>16.20 ± 0.65</td>
</tr>
<tr>
<td>22.9/5.71</td>
<td>32.90 ± 1.89</td>
<td>18.53 ± 1.86*</td>
<td>20.33 ± 1.25*</td>
<td>10.56 ± 0.59**</td>
</tr>
<tr>
<td>45.6/11.4</td>
<td>47.20 ± 3.70</td>
<td>21.43 ± 1.61*</td>
<td>22.38 ± 1.36*</td>
<td>12.68 ± 0.30**</td>
</tr>
<tr>
<td>91.4/22.9</td>
<td>56.88 ± 3.01</td>
<td>23.50 ± 1.36*</td>
<td>25.53 ± 1.58*</td>
<td>12.90 ± 0.58**</td>
</tr>
</tbody>
</table>

LPV/r = Lopinavir/ritonavir, MT = Melatonin, ALA = Alphalipoic acid. Results are expressed as mean ± S.E.M.  
*Significant (p<0.05) difference when compared to treatment with LPV/r  
** Significant (p<0.05) difference when compared to pretreatments with individual doses of MT and ALA

Table 5. Effects of MT and ALA on lopinavir/ritonavir-induced serum level of very low density lipoprotein cholesterol in male albino rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>LPV/r</th>
<th>MT+LPV/r</th>
<th>ALA+LPV/r</th>
<th>MT+ALA+LPV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12.23 ± 0.34</td>
<td>12.30 ± 0.34</td>
<td>12.30 ± 0.34</td>
<td>12.30 ± 0.34</td>
</tr>
<tr>
<td>22.9/5.71</td>
<td>24.90 ± 0.52</td>
<td>15.01 ± 1.06*</td>
<td>17.31 ± 1.07*</td>
<td>10.31 ± 2.18**</td>
</tr>
<tr>
<td>45.6/11.4</td>
<td>35.20 ± 2.64</td>
<td>16.22 ± 0.37*</td>
<td>20.23 ± 1.01*</td>
<td>11.05 ± 1.32**</td>
</tr>
<tr>
<td>91.4/22.9</td>
<td>43.88 ± 3.03</td>
<td>22.12 ± 1.21*</td>
<td>25.71 ± 2.09*</td>
<td>14.42 ± 0.04**</td>
</tr>
</tbody>
</table>

LPV/r = Lopinavir/ritonavir, MT = Melatonin, ALA = Alphalipoic acid. Results are expressed as mean ± S.E.M.  
*Significant (p<0.05) difference when compared to treatment with LPV/r  
** Significant (p<0.05) difference when compared to pretreatments with individual doses of MT and ALA
Table 6. Effects of MT and ALA on lopinavir/ritonavir-induced serum level of glucose in male albino rats

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>LPV/r</th>
<th>MT+LPV/r</th>
<th>ALA+LPV/r</th>
<th>MT+ALA+LPV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>50.75 ± 3.47</td>
<td>50.75 ± 3.47</td>
<td>50.75 ± 3.47</td>
<td>50.75 ± 3.47</td>
</tr>
<tr>
<td>22.9/5.71</td>
<td>71.00 ± 2.70</td>
<td>49.00 ± 2.70*</td>
<td>51.00 ± 2.81*</td>
<td>30.25 ± 2.75**</td>
</tr>
<tr>
<td>45.6/11.4</td>
<td>82.25 ± 4.62</td>
<td>51.25 ± 1.37*</td>
<td>50.00 ± 2.40*</td>
<td>30.75 ± 2.85**</td>
</tr>
<tr>
<td>91.4/22.9</td>
<td>110.25 ± 5.35</td>
<td>64.50 ± 3.25*</td>
<td>66.25 ± 4.75*</td>
<td>32.35 ± 1.10**</td>
</tr>
</tbody>
</table>

LPV/r = Lopinavir/ritonavir, MT = Melatonin, ALA = Alphalipoic acid. Results are expressed as Mean ± S.E.M.
*Significant (p<0.05) difference when compared to pretreatments with individual doses of MT and ALA
** Significant (p<0.05) difference when compared to pretreatments with combined doses of MT and ALA

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duced sterol regulatory element-binding protein (SREBP)-1c, as well as the expression of SREBP-1c target genes thereby preventing hepatic lipid accumulation (Chen et al., 2011). The observed decrease in GL level in MT pretreated rats could be attributed to the up-regulation of the activities of GLUT-4 (Zanquetta et al., 2003) and increase in GLUT-4 gene expression (Gosh et al., 2007). It has been shown to stimulate GL transport in skeletal muscle and improved glucose homeostasis by restoring the vascular actions of insulin (Ha et al., 2006). In addition, its effect on serum glucose level may be due to its ability to increase insulin output by stimulating pancreatic B–cells (Poon et al., 2001).

Furthermore, studies have associated increases in lipid and glucose levels with oxidative stress via free radical generation (Yang et al., 2008); hence effects of MT and ALA on lipid and glucose levels observed in the present study may be attributed to the antioxidant effects of MT and ALA (Cagnoli et al., 1995; Gitto et al., 2001; Rodriguez et al., 2004; Tan et al., 1994). Furthermore, several MT metabolites (e.g., N1-acetyl-N2-formyl-5-methoxykynuramine (AFMK) which could be formed when MT neutralizes damaging reactants are also free radical scavengers (Reiter and Korkmaz, 2008; Tan et al., 2007). Importantly, MT and ALA treatments could protect against mitochondrial damage there-by preventing the release of reactive oxygen species (Lopez et al., 2009; Paradies et al., 2010). In addition, MT and ALA have anti-inflammatory properties which might have contributed to their regulatory effects on lipid and glucose levels observed in this study (Odabasoğlu et al., 2011; Rodriguez et al., 2007). In the current study, decreases in serum lipid and glucose levels were highly pronounced in rats pretreated with combined doses of MT and ALA which could be attributed to synergy in the activity of MT and ALA (Adikwu et al., 2016).

Conclusion

This study showed that pretreatment with MT and ALA ameliorated LPV/r-induced increases in serum lipid and glucose levels. Maximum ameliorations were obtained with pretreatment using combined doses of MT and ALA. Based on observations in this study, MT and ALA could be used for the management of LPV/r associated alterations in serum lipid and glucose levels.

Acknowledgements

The authors appreciate the technical assistance of Mr. Woy Yirupe of the Department of Pharmacology, Faculty of Basic Medical Sciences, University of Port Harcourt, Choba, Rivers State.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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Eron, J., Yeni, P., Gathe, J., Estrada, V., DeJesus, E., Staszewski,
Beneficial effects of melatonin and alpha lipoic acid on lopinavir/ritonavir-induced alterations in lipid and glucose...


Резиме

Придобивки од третманот со мелатонин и алфа-липоична киселина при лопинавир/ритонавир-предизвикани промени на липидниот и гликозниот статус кај машки албино стаорци

Елиас Адикву*, Брамбаифа Нелсон, Волфе Атубоведиа Обианиме

Институт за фармакологија, Факултет за базични медицински науки, Универзитет на Порт Харкорт, Чоба, Нигерија

Ключни зборови: лопинавир/ритонавир, мелатонин, алфа-липоична киселина, липиден статус, гликоза, стаорци

Примената на лопинавир/ритонавир е поврзана со промени на нивоата на серумските липиди и гликоза. Актуелната студија е дизјанирана со цел да ги истражи ефектите на мелатонин (MT) и алфа-липоична киселина (ALA) врз лопинавир/ритонавир-предизвиканите промени на серумските нивоа на триглицеридите (TG), вкупниот холестерол (TC), липопротеините со ниска густина (LDL-C), липопротеините со многу ниска густина (VLDL-C) и гликозата (GL) кај машки албино стаорци. Стаорците од првата група, А1 (плацебо-контролирана) и втората група, А2 (третирана со растворувач), беа орално третирани со физиолошки раствор и 1% етанол, соодветно. Групите В, секоја со по 15 стаорци, беа орално третирани со MT (10 mg kg⁻¹/ден), ALA (10 mg kg⁻¹/ден) и нивна комбинација, соодветно. Стаорците во групата В беа поделени на 3 подгрупи, секоја со по 5 стаорци. Стаорците во групата В беа третирани орално со MT (10 mg kg⁻¹/ден), ALA (10 mg kg⁻¹/ден) и нивна комбинација, соодветно. Стаорците во групата С беа орално третирани со 22,9/5,71; 45,6/11,4 и 91,4/22,9 mg kg⁻¹/ден лопинавир/ритонавир, соодветно. Стаорците во групите D-F беа орално третирани со MT (10 mg kg⁻¹/ден), ALA (10 mg kg⁻¹/ден) и комбинирани дози на 22,9/5,71; 45,6/11,4 и 91,4/22,9 mg kg⁻¹/ден лопинавир/ритонавир, соодветно. Стаорците во групата В беа третирани во текот на 30 дена на крајот од третманот беа определени серумските нивоа на липидните фракции и гликоза. Третманот со MT и ALA значајно (p<0,05) ги намали почетните вредности на TG, TC, LDL-C и VLDL-C и GL, но овие параметри беа значајно (p<0,05) зголемени, дозно-зависно, кај стаорците пред третманот со лопинавир/ритонавир споредено со плацебо-контролираната група. Приемнатата на MT и ALA пред третманот со лопинавир/ритонавир значајно (p<0,05) ги намали серумските нивоа на TG, TC, LDL-C и VLDL-C и GL споредено со лопинавир/ритонавир-предизвиканите стаорци. Меѓутоа, намалувањата забележани кај стаорците претходно третирани со комбинација на МТ и ALA беа значајно (p<0,05) различни споредено со одделните третмани. Како заклучок, добиените резултати посочуваат дека комбинацијата MT и ALA може да го подобри липидниот и гликозниот статус променет под дејство на лопинавир/ритонавир.