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**College of: Science**  
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# **The Protective Role of Omega-3 and Melatonin Against $AlCl_3$ Induced some Biochemical Changes in Albino Rats**

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# INTRODUCTION

# Oxidative Stress

Oxidative stress (OS) is an imbalance between pro-oxidants and anti-oxidants leads to cell injury. This imbalance may be equivalent to the loss of homeostasis, occurs by weakening the antioxidant barrier represented by enzymes and non-enzymatic antioxidant factors, leads to accumulation of cytotoxic compounds, through an excess of pro-oxidant compounds that consume anti-oxidant reserves of the body (Sies, 1997).

# Aluminum

Aluminum (Al) is a potent neurotoxin that plays a pivotal role in the neuropathology of Alzheimer's disease (AD), prolonged Al exposure induces cognitive dysfunction, related oxidative damage and increases in deposition of beta amyloid ( $A\beta$ ) *in vivo* (Kumar *et al.*, 2009).

The toxic effects of Al may be due to the generation of reactive oxygen species (ROS), which is absorbed through the skin, gastrointestinal tract, lung and nasal mucosa, then accumulate in kidney, liver, brain and bone (Anand *et al.*, 2002; EL-Demerdash, 2004).

Regarding OS, it is possible that chronic administration of **poly unsaturated fatty acids** (PUFAs) may make the brain more vulnerable to lipid peroxidation, thus inducing antioxidative defense capacity and leading to elevated tolerance and protection against FR induced injury (Cao *et al.*, 2008).

**Melatonin** is a secretory product of the pineal gland and capable of preventing OS (Reiter *et al.*, 1995).

# Aims of Present Study

Since Al is added to drinking water for purification and accelerates oxidative damage to biomolecules like lipid, protein, nucleic acids and accumulates specially in brain which is more vulnerable to FR damage than other organs, the objectives of present study were to investigate:

The protective role of omega-3, melatonin and their combination against  $AlCl_3$  induced some biochemical changes especially (OS, lipid peroxidation and AD) markers in serum of experimental rats.

# **METHODOLOGY, RESEARCH DESIGN**

# Experimental Groups

Groups	Dose	Number of Rats (n)	Duration
G1: Control	-----	8	40 days
G2 : (AlCl <sub>3</sub> )	1000mg/L drinking water AlCl <sub>3</sub>	8	40 days
G3: (AlCl <sub>3</sub> +Omega-3)	1000mg/L drinking water AlCl <sub>3</sub> + 4g/ kg diet Omega-3	8	40 days
G4: (AlCl <sub>3</sub> +Melatonin)	1000mg/L drinking water AlCl <sub>3</sub> +50 mg/kg diet Melatonin	8	40 days
G5: (AlCl <sub>3</sub> +Melatonin +Omega-3 )	1000mg/L drinking water AlCl <sub>3</sub> + 4g/ kg diet Omega-3+ 50 mg/kg diet Melatonin	8	40 days



# Experimental Procedure



- **Body weight**
- **Brain weight**
- **Water intake**
- **Diet consumption**

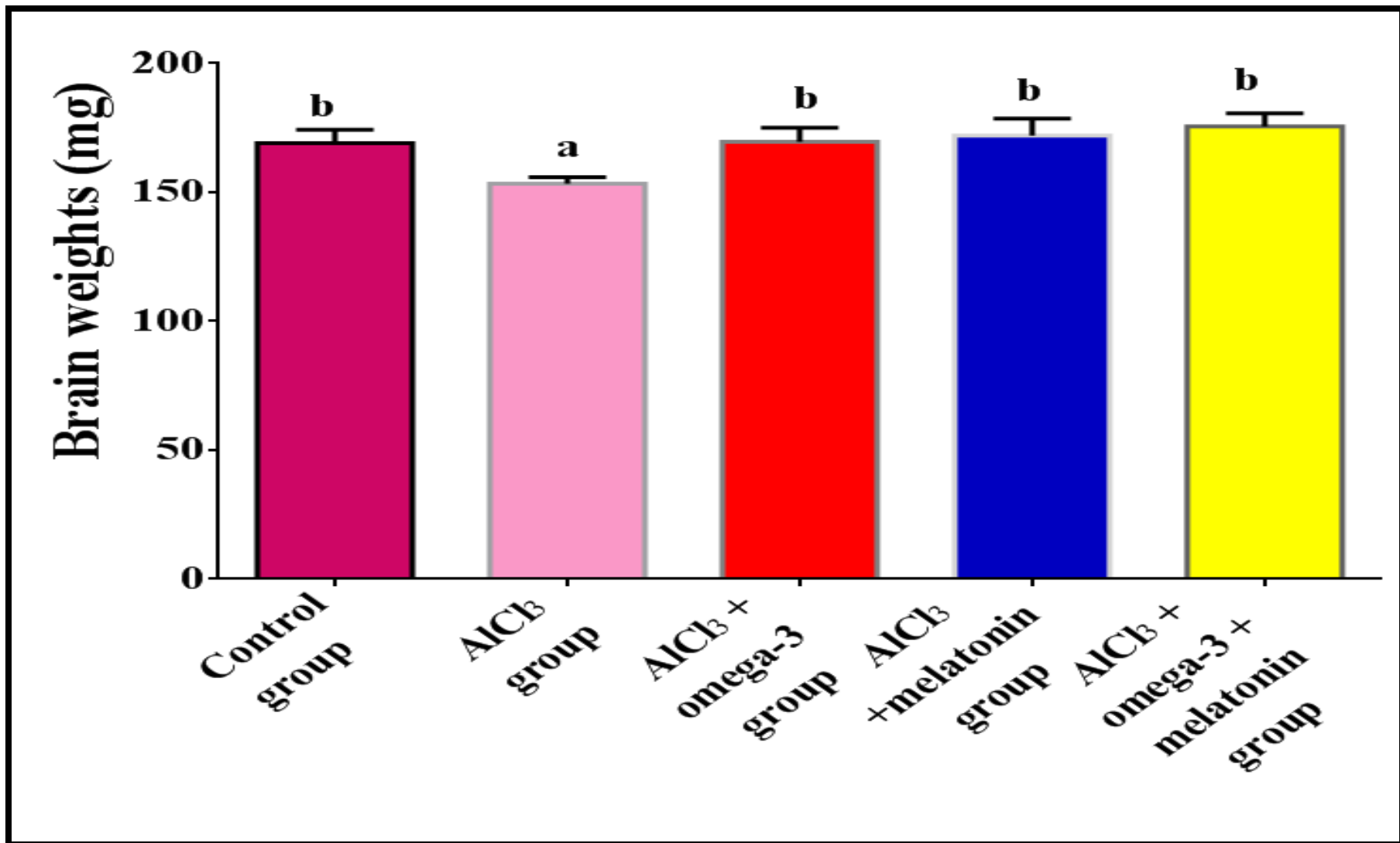


## Biochemical tests

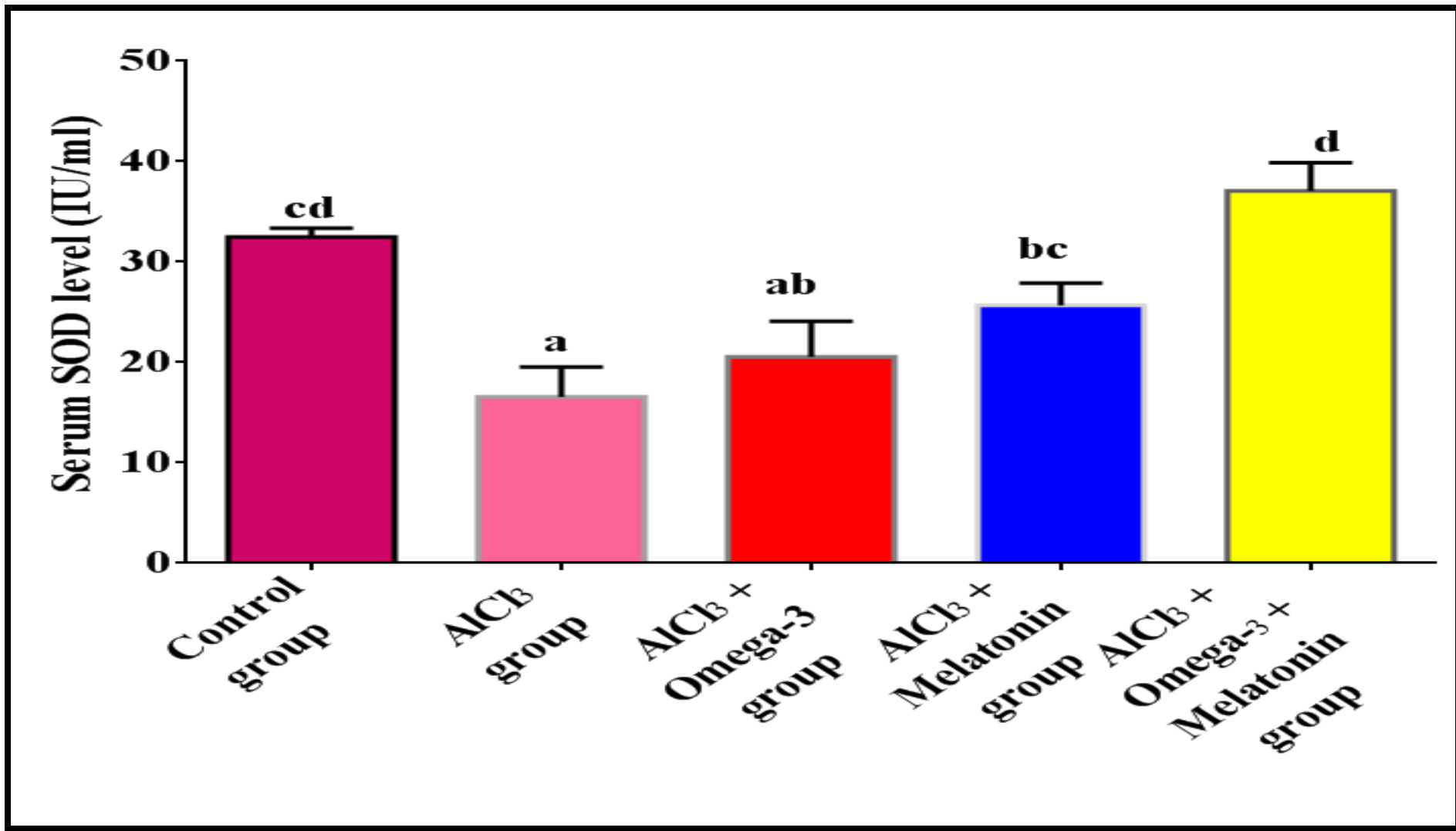


- **Serum**
  1. **SOD**
  2. **MDA**
  3. **A $\beta$  (1-42) peptide**
  4. **ALP, AST, ALT,**
  5. **Creatinine, Urea**
  6. **CK, LDH**
  7. **Glucose**

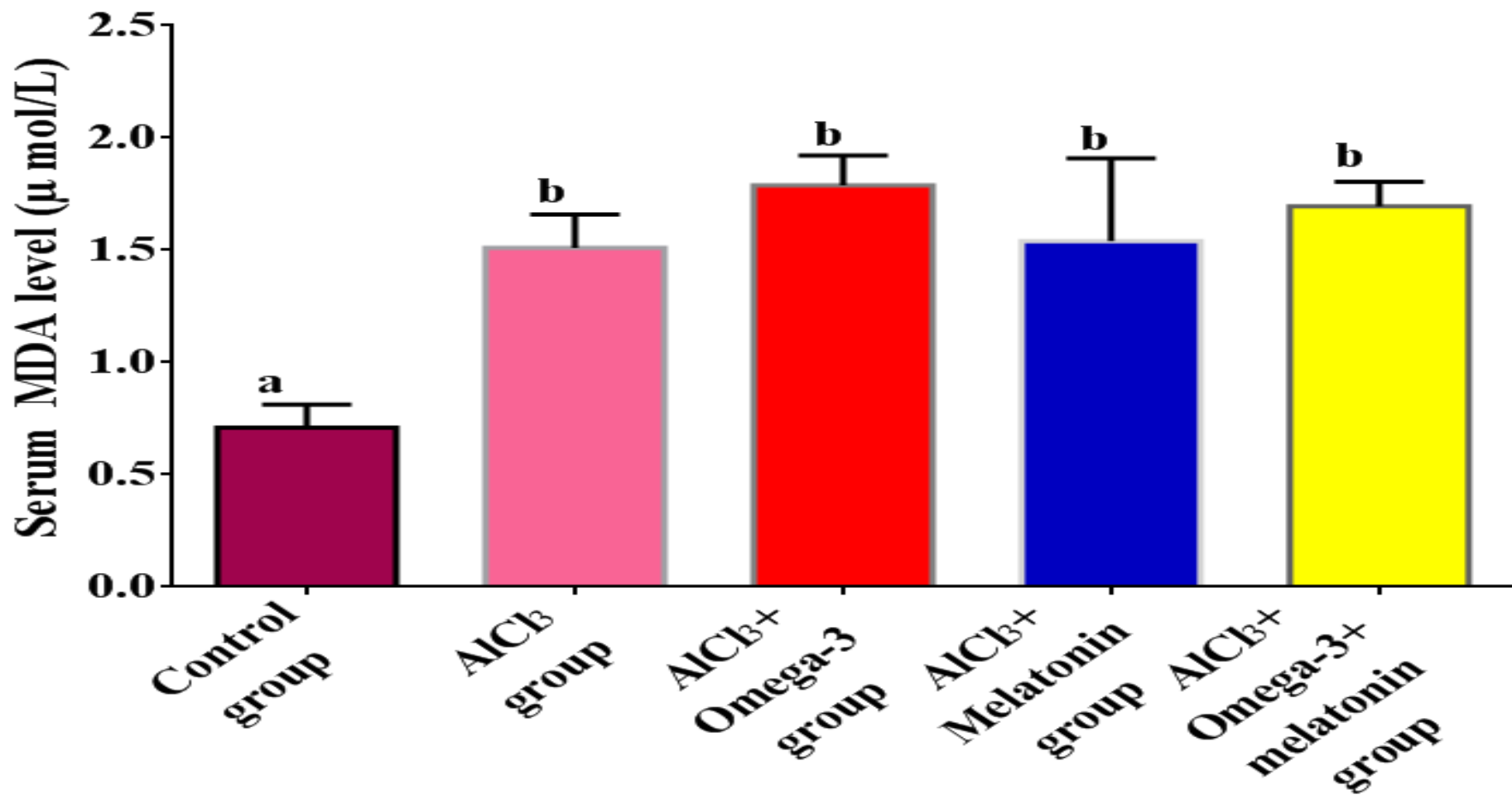
# **IMPLEMENTATION, RESULTS AND DISCUSSION**



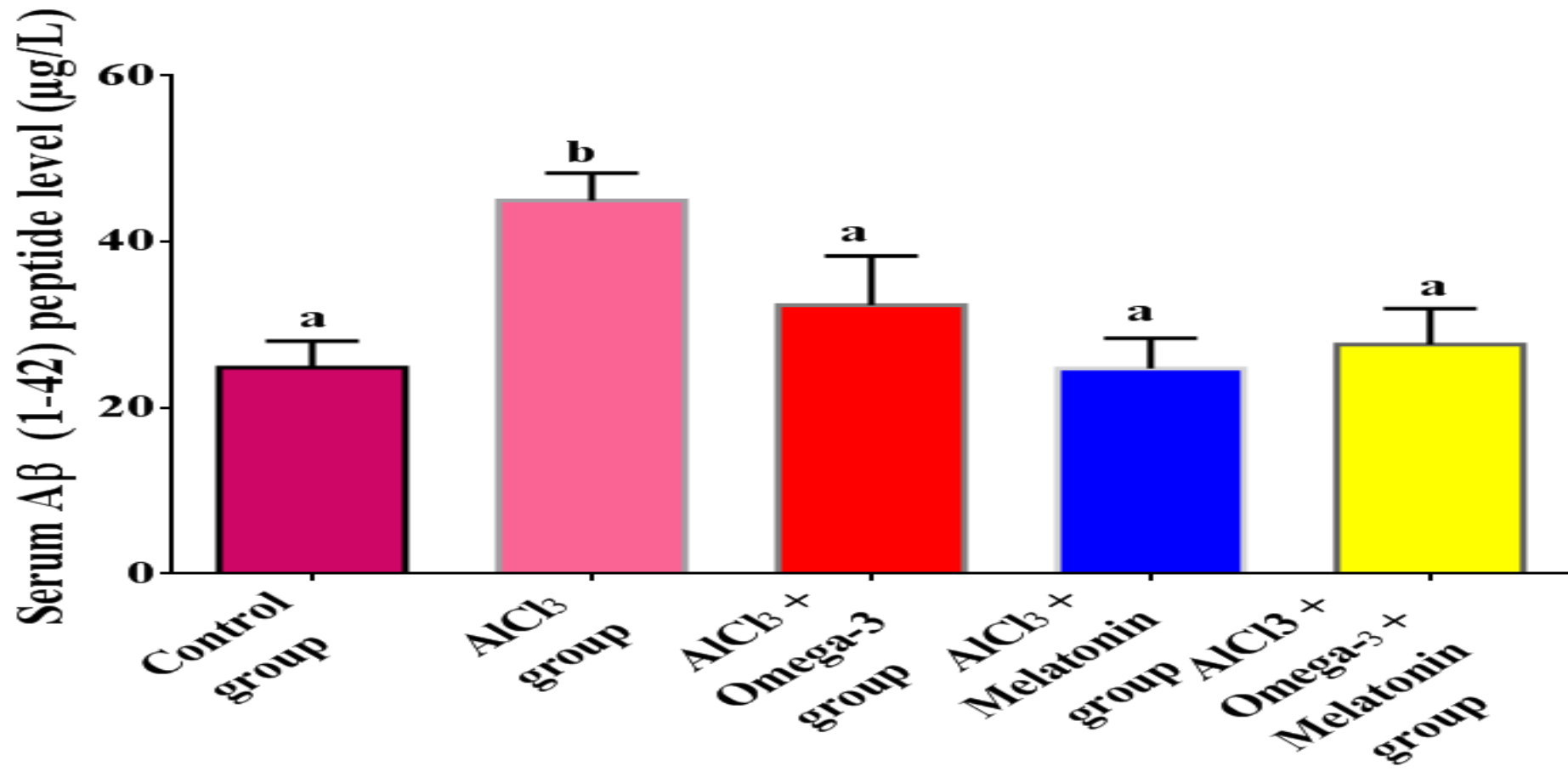
**Fig. 1. Effects of  $\text{AlCl}_3$ , omega-3, melatonin and their combination on brain weights of albino rats.**



**Fig. 2 : Effects of AlCl<sub>3</sub>, omega-3, melatonin and their combination on serum superoxide dismutase levels in albino rats.**

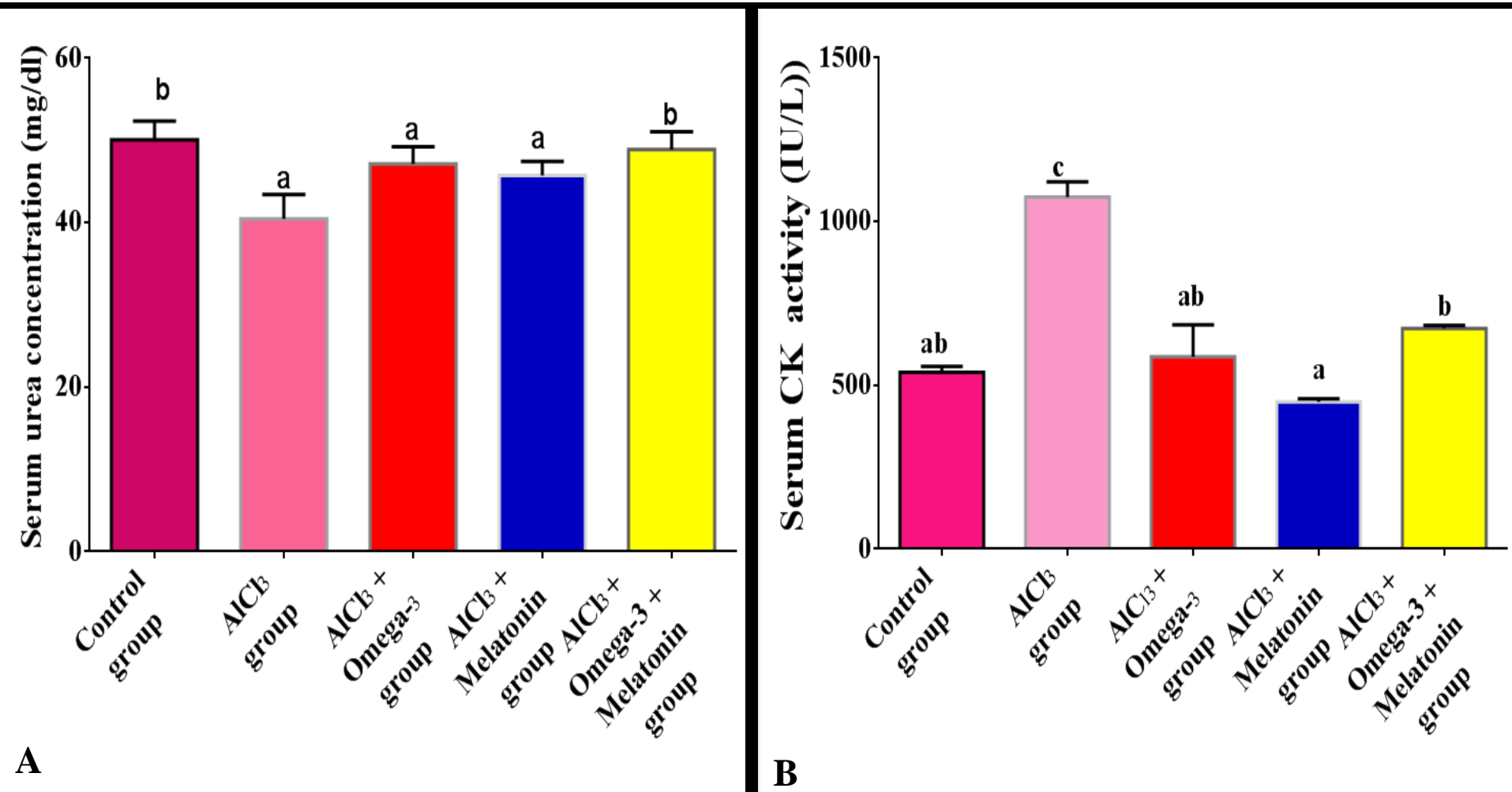


**Fig. 3 : Effects of  $\text{AlCl}_3$ , omega-3, melatonin and their combination on serum malondialdehyde levels in albino rats.**



A

**Fig. 4 : Effects of AlCl<sub>3</sub>, omega-3, melatonin and their combination on serum beta amyloid (1-42) peptide levels in albino rats.**



**Fig. 5. A and B: Effects of AlCl<sub>3</sub>, omega-3, melatonin and their combinations on serum urea concentration and creatine kinase activity in albino rats.**

- The results of biochemical study revealed that  $\text{AlCl}_3$  decreased SOD level while MDA and  $\text{A}\beta$  (1-42) peptide level increased.
- On the other hand, melatonin, omega-3 and their combination effectively increased SOD level except for omega-3 treated group in which no such effect detected on SOD level, while not affected on MDA level but decreased  $\text{A}\beta$  (1-42) peptide level.
- As well as CK activity increased in observed in  $\text{AlCl}_3$  group while treatment with melatonin, omega-3 and their combination ameliorate this effect.
- Additionally,  $\text{AlCl}_3$  unexpectedly decreased urea concentration, only combination of omega-3 and melatonin normalized urea concentration.
- Sub-acute dose of  $\text{AlCl}_3$  did not cause any significant effect on serum ALP, AST, ALT creatinine, LDH and glucose levels.



**CONCLUSIONS  
AND  
RECOMMENDATIONS**

# CONCLUSIONS

1. Oxidative stress responsible for brain atrophy but melatonin, omega-3 either alone or together protects against brain weight loss by protecting large number of healthy neurons from oxidative damage through their antioxidant role, while sub-acute dose of  $\text{AlCl}_3$  (1000mg/L drinking water) has no effect on appetite hence not affect on body weight.
2. Aluminum chloride caused biochemical alterations in serum female rats, while melatonin, omega-3 either alone or together could protect against OS through their antioxidant and anti-amyloidal role in response to Al toxicity.

3. Aluminum chloride causes myocardial and neuronal damage by enhancing FR generation leading to inactivate NO level subsequently leads to vasoconstriction and increases CK activity, while melatonin, omega-3 and their combinations ameliorate these effects by FR scavenging ability.
4. The main mode of cell death in response to Al is necrosis in the brain while in the liver and kidney may be apoptosis through the action of FRs.  $AlCl_3$  affects on protein metabolism, while combination of omega-3 and melatonin ameliorate this effect.

# RECOMMENDATIONS

1. Further studies are recommended to find out the histopathological and biochemical changes associated with OS in other parts of the brain and in other organs especially liver, kidney, lung and heart, as well as their homogenate, where Al accumulates there.
2. Finding the most suitable dose and duration for using omega-3, melatonin and their combinations against  $AlCl_3$  exposure.
3. More studies are required to investigate the interaction among  $AlCl_3$ , omega-3, melatonin and hormones especially female sex hormones since deficiency in the hormones like estrogen deprivation likely to induce diseases like AD.
4. Avoids Al exposure through inhalation, oral exposure by water and foods containing this metal. Prevents using Al utensil for food preparation and drugs that contain Al compounds.
5. It is better to do experiments on male rats and ovariectomized rats in order to avoid any hormonal fluctuations that may affect on biochemical results.

**Thanks for your Attention**

