



Effectiveness of Turmeric and Extra Virgin Olive Oil in the Management of IL 6 and IL 10 in Healthy Mice

Sama Mohammed Attiyah¹ and Hoda Elsayed Mohammed^{1*}

¹*Biology Department, Faculty of Sciences and Arts, Al Kamel Branch, University of Jeddah, Jeddah, Saudi Arabia.*

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Anti-inflammatory properties of turmeric and extra virgin olive oil have numerous health benefits. They exert and promote anti-inflammatory actions, moreover, each gives benefits that go beyond reducing inflammation.

Objective: The aim of our study is to evaluate and compare the immunomodulatory effect of each turmeric and extra virgin olive oil (EVOO) alone or in combination.

Methods: We demonstrated the serum level of pro-inflammatory cytokines IL-6 and IL-10 in healthy male Swiss albino mice (C57BL/6 strain) after oral intake of curcumin and extra virgin olive oil for six weeks by ELISA assay.

Results: Our results showed that dietary intake of turmeric and EVOO had a reducing effect on serum IL-6 level and could increase the production of IL-10 level significantly. Inflammatory responses of turmeric and EVOO combination appear to be more effective on health by inhibition of IL 6 and induce IL 10 production.

Conclusion: Anti-inflammatory effect of turmeric and EVOO can play an important role in modulating the level of IL 6 and IL-10. Moreover, co-administration of them having a greater anti-inflammatory effect.

Keywords: *Turmeric; extra-virgin olive oil; pro-inflammatory; anti-inflammatory; IL-6; IL-10; cytokines.*

1. INTRODUCTION

Several countries rely on their diet on extra virgin olive oil and turmeric or both together such as the Mediterranean and Asian citizens. Olive oil and turmeric contribute to enhance immune system function against disease especially inflammatory and infection types. Each of these spices is reported previously as anti-inflammatory, anti-cancer, antiviral, antifungal, and antioxidant elements [1,2].

The intake of extra virgin olive oil diet patterns has been linked to a variety of health benefits [3]. Researchers found that Mediterranean people present a lower risk of cancer and they found the relation between olive oil and the inhibition of specific cancer types [4,5]. Furthermore, several studies indicate the bioactive effect of olive oil on the secretion of pro and anti-inflammatory cytokines such as IL-4, IL-10, TNF- α , and IFN- γ [6,7].

Extra virgin olive oil's health benefits have been related to the presence of phenolic compounds and monounsaturated fat content, which have antioxidant, anti-inflammatory, and immunomodulatory qualities which responsible for diet's health advantages [8,9]. Furthermore, long-term consumption of the oil is linked to a decrease in inflammatory biomarkers [10].

On the other hand, the yellow pigments identified from *Curcuma longa* in curry named curcumin or turmeric is one of the most interesting spices that have health advantages properties [11,12]. It is a traditional spice in India and Chania diet and is involved in their medicine as well. Chinese and Indian people showed good health conditions and they were able to fight various infections, inflammation, and cancer better than other populations. Scientists found that turmeric has bioactive components that work as anti-inflammatory and antioxidant factor that suppress the development of some diseases [2]. Researchers found turmeric able to fight virus replication and inflammation by boosting the immune system, and leading to decrease infection symptoms [11]. It is also considered as antioxidant, anti-inflammatory and probably anticancer as well, that provide reduction consequences in inflammation and infection [4, 11,13]. One of the most significant drawbacks of consuming curcumin alone is 1. Low bioavailability due to its poor absorption, 2. Rapid metabolism, 3. Rapid elimination. Piperine is one

of the bioavailability enhancers that can increase the bioavailability of curcumin [14].

Regarding turmeric, Hui and his group revealed that the enhancement of turmeric to reduce IL-6 and IL-8 concentration is not significant which requires more investigation [11]. Curcumin plays an important role in decreasing the cytokine storm attack through inflammation or infection in humans [15]. Likewise, this was reported by other studies that showed cytokines production blocked inflammation due to curcumin reaction representing decreasing and enhancement in pro-inflammatory and anti-inflammatory cytokines (IL-1, IL-8, IL-10 & COX-2) [2,13]. The capability of curcumin to inhibit and decrease pneumonia and Ebola incident in human have been studied previously [13,15]. Scientists should concentrate on the beneficial role of curcumin in relieve coronavirus symptoms and decrease the incident as well for COVID-19 [13,16].

Our research was carried out to evaluate the immunomodulatory response of EVOO and turmeric as an anti-inflammatory agent and their co-administration effect on healthy Swiss albino mice (C57BL/6 strain) by assessing IL 6 and IL 10 serum levels.

2. METHODOLOGY

2.1 Animals

A total of 48 healthy male Swiss albino mice (C57BL/6 strain) aged 6-8 weeks and weighing 20-30 gm were used. The animals that used obtained in Egypt from the European Country Farms. Mice were thoroughly inspected to verify that no symptoms of microbiological or parasite illnesses were present. They were housed in Theodor Bilharz Research Institute (TBRI) in suitable plastic cages under a temperature of 21 C° and 60% humidity. Moreover, they were kept on a standard diet containing 24% protein, 4% fat, 4-5% fiber, and water ad-libitum. The animals were fed, housed, and handled in accordance with the recommendations of (Gide For Care And use Of Laboratory Animals).

2.2 Experimental Design

Briefly, mice were allocated into 4 groups (12 animals/group). The first group was allocated to a control group. The control group administrated just water with the standard diet. Turmeric group administrated 2 gm turmeric and 20 mg piperine

/kg body weight. Olive oil group that administrated with daily consumption dose amount of 0.2ml olive oil/25gm body weight. Turmeric/Olive oil group administrated 2 gm turmeric and 20 mg piperine /kg and 0.2ml olive oil/25gm. The bioavailability of curcumin was improved by the combination of piperin and turmeric. In our study, we increased the bioavailability of turmeric by its combination with piperin.

All the doses administrated by P.O. gavage daily for 6 weeks. After 2 weeks, 4 weeks, and 6 weeks, four mice from each group were slaughtered. Each interval period, serum levels of IL 6 and IL 10 were measured.

2.3 Assessment of Interleukins (IL-6 and IL10) by ELISA

Blood samples were collected, allowed to clot at room temperature, and then centrifuged for 15 minutes at 4000 rpm. Serum samples were taken and kept at -80 °C until needed. Both tests were carried out using the sandwich-ELISA technique. Commercial ELISA kits were used to measure IL10 (NOVA Rat interleukin ELISA kit cat #: In Ra0655) and IL6 ((China and Cloud Clone Corp. IL6 ELISA kit cat #: E-20303Mo) in accordance with the manufacturer's instructions.

2.4 Statistical Analysis

SPSS statistical package was used for data analysis, version 20 with Excel programming software used for tabulating and showing the data. All results were expressed as mean± SD. The significant difference between groups was noted using a one-way analysis of variance (ANOVA). P- values < 0.05 were considered significant.

3. RESULTS

The current study revealed significant inhibition of IL-6 release through oral administrations of each turmeric and extra virgin olive oil after 6 weeks and 4 weeks, and co-administrations of turmeric with EVOO revealed a significant decrease after the second week respectively ($P < 0.05$). The effect of prolonged daily co-administrations of turmeric with extra virgin olive oil showed a significant decrease in serum IL-6 level ($P < 0.001$). Our findings reported in Table 1 depicted the serum IL-6 level for each group. Co-administration of turmeric and extra virgin olive oil showed a modest decrease of IL-6 than if they were administrated separately. The serum IL-6 levels throughout the study time interval are shown in Fig. 1. It showed a statistically significant difference between the groups' IL-6 levels.

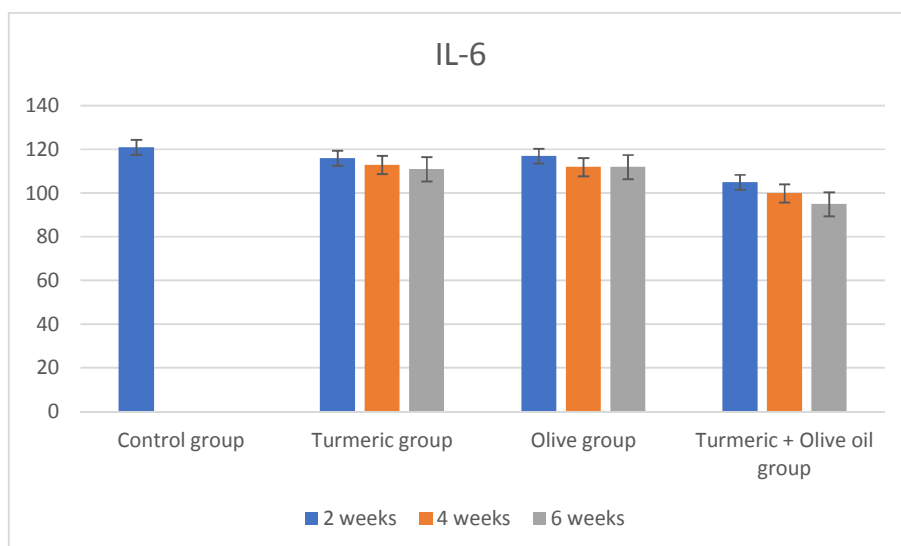


Fig. 1. Comparative bar diagram showing IL-6 levels in healthy female swiss albino mice with daily oral intake of turmeric, extra virgin olive oil and their combination after 2 weeks, 4 weeks and 6 weeks

Table 2 showed a significant increase in serum IL-10 relative to the control of the study. All groups induced the production of IL-10. Moreover, changes in IL-10 level were strongly significant through a prolonged experiment administration interval period. We observed a

significant increase in IL-10 levels of serum with turmeric administrated supplements after 2 weeks ($p < 0.05$) which increased markedly after 6 weeks as well as their prolonged combination ($P < 0.001$). Fig. 2 showed that all potent and efficacious data in promoting IL-10 production.

Table 1. Changes in IL-6 level throughout the study

	IL-6		
	2 weeks (Mean ± SD)	4 weeks (Mean ± SD)	6 weeks (Mean ± SD)
Turmeric group	116± 3.3	113±3.5	111±2.9*
Olive oil group	117±2.6	112±2.4*	112±3.2*
Turmeric + Olive oil group	105±2.5*	100±2.6**	95±2.1**

*Results have been presented as mean ± standard deviation of four samples (n = 4). Significant effects are indicated by asterisks (*P < 0.05, **P < 0.001)*

Table 2. Changes in IL-10 level throughout the study

	IL-10		
	2 weeks (Mean ± SD)	4 weeks (Mean ± SD)	6 weeks (Mean ± SD)
Turmeric group	220±7.1*	270±6.8*	442.5±9.1***
Olive oil group	261±6.8**	282.5±6.1**	305.5±7.2***
Turmeric + Olive oil group	234.5±4.5*	346.5±4.2***	521±3.2***

*Results have been presented as mean ± standard deviation of four samples (n = 4). Significant effects are indicated by asterisks (*P < 0.05; ** P < 0.01; *** P < 0.001)*

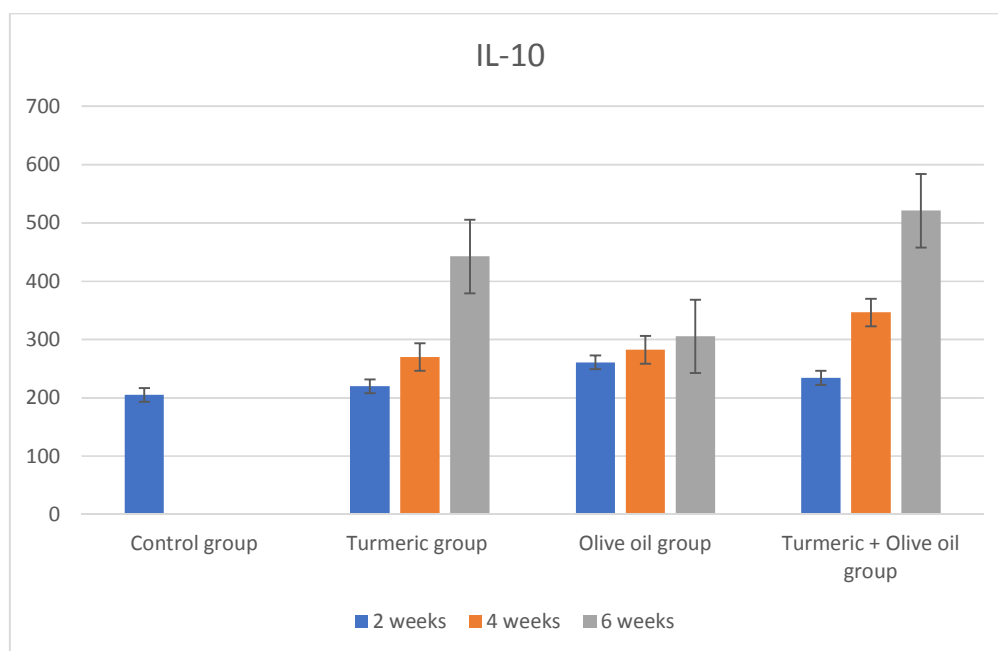


Fig. 2. Comparative bar diagram showing IL-10 levels in healthy female swiss albino mice with daily oral intake of turmeric, extra virgin olive oil and their combination after 2 weeks, 4 weeks and 6 weeks

4. DISCUSSION

The anti-inflammatory effect of turmeric and extra virgin olive oil provoked interest in several scientific research and has been discovered to have antioxidant and anti-inflammatory properties and many other diet's health benefits. Each can alter the human immune system by influencing the release of interleukins involved in immunological defense [17,18,19].

The bulk of turmeric as well as extra virgin olive oil studies too far have been conducted in populations who already have health issues. Our study was directed to verify their effect on pro- and anti-inflammatory cytokines after consumption for sex weeks separately or in combination in healthy mice. To the best of our knowledge, this is the first study to demonstrate their positive benefits in healthy conditions.

One research on healthy people who took curcumin for four weeks showed the inflammation related to neutrophil activity was improved significantly [20]. Moreover, a pilot investigation on healthy people found that using olive oil reduced IL-6 levels and hence decreased systemic inflammation [21].

The impact of turmeric and its key component curcumin on anti-inflammatory cytokines have been established in several researches on inflammatory disorders. Many studies have linked its impact to a decrease of IL-6 levels in the blood [22,23], while other studies revealed that curcumin did not substantially lower the level of IL-6 [11,24]. Moreover, curcumin has also been shown in other studies to increase the level of IL-10, which can regulate the immune response in inflammatory situations [25].

Several studies have been previously examined the anti-inflammatory properties of EVOO consumption. They found that its supplementation led to a significant decrease of IL6 level [26,27,28], while increased IL-10 level [28].

The observed anti-inflammatory effects of turmeric and EVOO dietary intervention may be due to inhibition of COX-1 and COX-2 to prevent the production of the eicosanoids prostaglandin E2 and 5-hydroxyeicosatetraenoic acid [29]. More research is needed to clarify these issues.

In our study, we have assessed blood IL-6 levels and IL-10 after two, four and, sex weeks with daily oral administration by turmeric and EVOO each one separately and in combination. Although each one can induce an anti-inflammatory response by reducing blood IL-6 levels and raised IL-10 production levels. Furthermore, the current study presents significant changes in anti-inflammatory cytokines level relatively prolonged duration time. Our main observation was that the consumption of the mixture of turmeric and extra virgin olive oil can induce a strong immunomodulatory response with a more significant effect on IL-6 and IL-10 blood levels than when each is consumed separately.

It should be emphasized that the immunomodulation demonstrated by the turmeric and EVOO combination in healthy conditions requires more research to corroborate our findings with some inflammatory diseases.

5. CONCLUSION

This study revealed that prolonged administration of turmeric and extra virgin olive oil can influence the levels of anti-inflammatory cytokines such as IL 6 and IL 10. Moreover, their combination is more effective and significant to the immunomodulatory system.

6. LIMITATIONS

One of our potential limitations to this study that should be revealed; other anti-inflammatory markers were not assessed, which may further highlight the concurrent effects on other anti-inflammatory cytokines. Furthermore, the study's other limitations include a small sample size.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was approved by Research Ethics Committees (TBRI-REC), TBRI, Egypt, approval number is IP987370/2021. They were recognized by an animal ethics institution for the care of animals and the safe disposal of their wastes at TBRI.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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