

Exploring the immunomodulatory potential of Ceylon organic black tea through in vivo studies using a mouse model

¹Premantha, H.K.H.M., ¹Shashika, M., ¹Mendis, B.I.L.M., ¹Palihaderu, P.A.D.S.,

²Wanasinghe, K.D.K., ³Premarathne, J.M.K.J.K., ⁴Wijesundara, K.K., ⁵Alles, N.,

¹Jayasooriya, A.P. and ^{1,*}Satharasinghe, D.A.

¹Department of Basic Veterinary Sciences, Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, Peradeniya, Sri Lanka

²English Teashop (UK) Ltd, 5th Floor, 3 Dorset Rise, London, EC4Y 8EN, United Kingdom

³Department of Livestock and Avian Sciences, Faculty of Livestock, Fisheries, and Nutrition, Wayamba University of Sri Lanka, Makandura, Gonawila (NWP), Sri Lanka

⁴Department of Veterinary Pathobiology, Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, Peradeniya, Sri Lanka

⁵Department of Biochemistry, Faculty of Medicine, University of Peradeniya, Peradeniya, Sri Lanka

Article history:

Received: 21 July 2025

Revised: 17 September 2025

Accepted: 10 October 2025

Published: 7 April 2026

Keywords:

Ceylon organic black tea,
Immunomodulatory effect,
Cytokines,
Network effect,
Wellness

DOI:

[https://doi.org/10.26656/fr.2017.10\(2\).170-5](https://doi.org/10.26656/fr.2017.10(2).170-5)

This open access article is licensed under the CC BY 4.0



Abstract

Black tea is one of the most popular beverages worldwide, derived from *Camellia sinensis*. Bioactive molecules, including polyphenols, flavonoids, alkaloids, free amino acids, polysaccharides, and saponins, are rich in black tea. These bioactive molecules contribute to the anti-inflammatory, anticancer, immunomodulatory, and cardiovascular protective effects. This study aimed to determine the immunomodulatory and toxicity effects of organically grown Ceylon black tea in a mouse model. Black tea infusion was orally administered to mice at the recommended animal dose for six days. Milliplex® Map 38-plex human cytokine/chemokine magnetic bead-based panel and Luminex® MAGPIX® platform were used to determine the expression levels of GM-CSF, IFN- γ , IL-2, IL-4, IL-6, IL-10, IL-12 (p70), TNF- α , MIP-1 β , and RANTES in selected time points. The results indicated immunomodulatory effects in the Ceylon organic black tea-treated group compared to the controls. Therefore, the current study highlights the immunomodulatory potential of organic black tea, demonstrating its ability to regulate key cytokine expression levels in a controlled and balanced manner. According to the findings of the histopathological examination, animals treated with Ceylon organic black tea for 28 days showed normal healthy morphology similar to that of the control group. The present study suggests that black tea exhibits an immunomodulatory effect and is safe for regular consumption, especially at 2 g/per animal. By comprehensively evaluating both immunomodulatory and toxic effects of Ceylon organic black tea, this study has contributed novel insights to the field.

1. Introduction

Tea is the second most widely consumed beverage worldwide, after water, and plays a significant role in global culture and health (Preedy, 2013; Naveed *et al.*, 2018). Tea is prepared from the leaves of *Camellia sinensis*, originating as a medicinal drink in the Chinese province of Yunnan (Suzuki *et al.*, 2016). China is the largest tea producer in the world, followed by India, Kenya, and Sri Lanka (Ridder, 2025). Different tea varieties can be produced based on the process used to obtain the degree of fermentation, including black tea, oolong tea, green tea, yellow tea, dark tea and white tea

(Sharma and Rao, 2009; Tang *et al.*, 2019).

Black tea is the most popular type of tea, accounting for approximately 75–80% of global tea consumption (Sharangi, 2009; Preedy, 2013). Unlike green or white tea, black tea undergoes complete oxidation, which takes about 2–4 hours, depending on the temperature and humidity. The oxidation of polyphenolic compounds enhances the colour, flavour, and bioactive compound profile of black tea (Sharma and Rao, 2009).

Black tea is rich in bioactive compounds, including polyphenols, catechins, theaflavins, thearubigins,

*Corresponding author.

Email: dilansatharasinghe@vet.pdn.ac.lk

alkaloids (such as caffeine, theobromine, and theophylline), and amino acids like theanine (Dou, 2019; Tang *et al.*, 2019). Catechins are the primary type of polyphenol, while theaflavins and thearubigins are considered the primary pigments in black tea (Li *et al.*, 2013; Dou, 2019).

These compounds contribute to its strong antioxidant, anti-inflammatory, immune-modulatory, anti-diabetic, anti-obesity, cardiovascular-protective, and anti-cancer properties (Sharangi, 2009; Tang *et al.*, 2019). Research has also shown that black tea consumption may support gut health, enhance cognitive function, and reduce the risk of chronic diseases (Li *et al.*, 2013; Dou, 2019). The dietary flavonoids in black tea provide health benefits with anti-viral, anti-inflammatory and anti-bacterial responses against various infectious agents (Sharangi, 2009; Chattopadhyay *et al.*, 2012).

A properly functioning immune system is essential for preventing infectious diseases, promoting recovery from illness, and maintaining overall health and well-being (Parkin and Cohen, 2001). Cytokines are small, secreted proteins that act as key signalling molecules in the immune system, playing crucial roles in innate and adaptive immunity, orchestrating cellular communication, immune cell activation, differentiation, and migration. Their functions span across innate immunity, humoral immunity, and cell-mediated immunity, making them central to immune regulation and response. Innate immunity is the first line of defence and relies heavily on cytokines to mount a rapid, nonspecific response to pathogens. Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) promotes myeloid cell proliferation and activation of macrophages and dendritic cells. GM-CSF promotes the differentiation of granulocytes and monocytes and enhances antigen-presenting cell function and the expression of Major Histocompatibility Complex (MHC). Pro-inflammatory cytokines such as tumour necrosis factor- α (TNF- α), interleukin-1 (IL-1), and IL-6 are produced by macrophages, dendritic cells, and other innate cells in response to pathogen-associated molecular patterns (PAMPs). They promote inflammation, fever, and acute-phase responses. IL-12 (p70) induced Th1 differentiation and IFN- γ production, leading to activation of natural killer (NK) and cytotoxic T cells (Murphy and Weaver, 2017). MIP-1 β (CCL4) chemotaxis of monocytes and lymphocytes that recruit inflammatory cells to the site of infection (Abbas *et al.*, 2018). RANTES (CCL5) bridges innate and adaptive responses by attracting T cells, eosinophils and basophils critical for inflammation (Von Luetichau *et al.*, 1996). Humoral immunity, primarily mediated by B cells and

antibodies, is regulated by cytokines produced by T helper cells and other immune cells. IL-4, IL-5, and IL-6 are critical for B cell proliferation, differentiation, and antibody class switching. For example, IL-4 promotes class switching to IgE, which is important in allergic responses (Le Gros *et al.*, 1990). TNF and IL-6 also influence the development of plasma cells and the production of high-affinity antibodies. IL-10 is a regulatory cytokine that suppresses macrophage and dendritic cell functions and is important in innate and humoral immunity. Cell-mediated immunity is a key arm of adaptive immunity. IFN- γ activates macrophages and polarises T helper cells towards a Th1-like response. IL-2 is critical for T cell clonal expansion and NK cell activation (Abbas *et al.*, 2018).

Considering the increasing burden of infectious diseases and lifestyle-related disorders, strengthening the immune system through natural and holistic approaches is increasingly important. Research into dietary and botanical interventions continues to provide valuable insights into how the immune system can be effectively supported, ultimately contributing to improved public health outcomes (Calder *et al.*, 2020). A recent narrative review based on published papers in English from 1990 to 2024 on clinical trials for the health benefits of black tea, focusing on cardiovascular and metabolic health and cognitive function, indicated that consuming black tea regularly enhances endothelial and vascular health, notably by improving flow-mediated vasodilation (Yilmaz, 2025). However, numerous studies have described the health benefits of black tea (Sharangi, 2009; Sharma and Rao, 2009); the assessment of immune functions through functional proteins like cytokines in vivo models is limited and conducted in a short period. Therefore, this study aimed to determine the immunomodulatory effect through direct quantification of cytokines expressed in plasma and the toxicity effects of Ceylon organic black tea in a mouse model.

2. Materials and methods

2.1 Ethical approval

All experiments involving animals were conducted in accordance with national and international regulations and guidelines for the use of laboratory animals. The study protocol was approved by the Faculty Ethics Committee, Faculty of Veterinary Medicine and Animal Science, University of Peradeniya (VERC21-19).

2.2 Experimental animals and sample collection

Six-week-old male Balb/c mice were purchased from the Medical Research Institute, Colombo, Sri Lanka and acclimatised to the new environmental conditions for

two weeks. The animals were maintained in the animal house at the Faculty of Medicine, University of Peradeniya, under controlled conditions of 24-28°C, 65-80% relative humidity, and a 12-hour light/dark cycle. Animals were housed in clean polypropylene cages using wood shavings as bedding material and fed AIN-93G purified rodent diet (Dyets, Inc., USA) and distilled water ad libitum. All the animals were kept in germ-free conditions and were not fasted at any time.

2.3 Preparation and administration of organic black tea to animals

Certified organic black tea manufactured according to European Commission Standards and Regulations (EC) No 834/2007, provided by English Teashop (UK) Ltd's manufacturing arm based in Sri Lanka, was used for the experiment.

The weight of Ceylon organic black tea for the human dose was considered as one tea bag with 2 g of tea for three times per day and prepared in 240 mL (1 cup) of freshly boiled water for 5 min. Certified organic dried black tea was received from the manufacturing arm of the English Teashop (UK) Ltd, which is based in Sri Lanka. The weight of Ceylon organic black tea for the human dose was considered as 2 g in one tea bag for three times a day and prepared in 240 mL (1 cup) of freshly boiled water for 5 mins. The weight of tea at once and the times of consumption were considered as the average values (Zhang *et al.*, 2022).

The required dose of organic black tea for oral treatment of mice corresponding to the human equivalent dose (HED) was calculated using the formula described by Diehl and colleagues (Diehl *et al.*, 2001).

The mice were divided into three groups (n= 10) for negative, positive controls and treatment. The negative control group received distilled water while the positive control group received an immunostimulant, Levamisole hydrochloride solution (Levoral 75% W.S.P., Dutch Farm International BV, Holland) (Gholami *et al.*, 2023). All the solutions were administered orally using a 22G mouse feeding needle at a single dose volume of 0.5 mL three times per day in 4-hour intervals. The overview of the experiment is indicated in Figure 1.

2.4 Gross observations after treatments

During the experiments, the animals were continuously monitored under veterinary care to detect any behavioural or clinical abnormalities such as excitement, vomiting, diarrhoea, altered feeding, sleep and ataxia. The daily body weights were also recorded at a selected time each day. The body weight at the beginning of the experiment was considered as the initial

weight, and the body weight at the end of the experiment was considered as the final body weight.

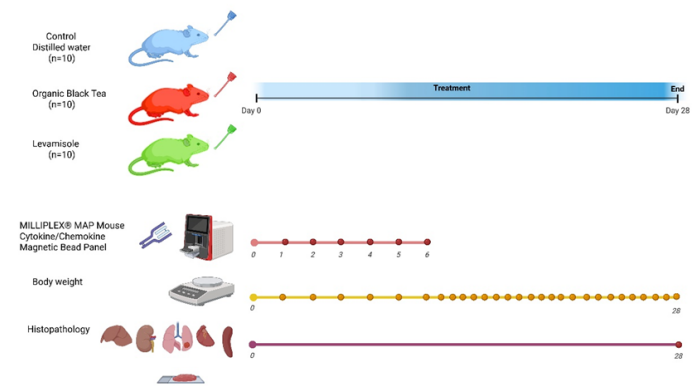


Figure 1. Overview of the experiment.

2.5 Determination of selected cytokine levels

Blood samples were collected at 0 h, 24 h, 48 h, 72 h, 96 h, 120 h and 144 h after starting treatments from tail tip amputation under anaesthesia. The blood samples were collected into K3EDTA-coated micro blood collection tubes. Collected blood samples were centrifuged for 10 minutes at 1000 g within 30 minutes of blood collection, and the separated plasma was stored at -20°C until further analysis.

The cytokines were selected by considering their specific functions related to innate, humoral, and cell-mediated functions (Table 1). The GM-CSF, IFN- γ , IL-2, IL-4, IL-6, IL-10, IL-12 (p70), TNF- α , MIP-1 β , and RANTES were determined using a customised MILLIPLEX® MAP Mouse Cytokine/Chemokine Magnetic Bead Panel (MCYTOMAG-70K, Merck KGaA, Darmstadt, Germany) following the manufacturer's protocol. The expressed cytokines were analysed using Belysa software version 1.1 (Merck, Germany) at a recovery range of 80% to 120% with a 20% coefficient of variation limit.

Table 1. Assessed cytokines and the target type of immune response.

Immunity type	Cytokines
Innate immunity	GM-CSF, IL-10, TNF- α , MIP-1 β ,
Humoral immunity	IL-4,
Cell-mediated immunity	IFN- γ
Innate and humoral immunity	IL-6, IL-10,
Innate and cell-mediated immunity	IL-12 (p70), RANTES (CCL5)

2.6 Histopathology

After 28 days of experiment, animals were sacrificed using sodium pentobarbitone, and kidney, liver, heart, spleen, and lung samples were collected for necropsy. All organ samples were preserved in 10% neutral buffered formalin. The tissue sections were cut and

processed using a tissue processor (SHANDOM Elliott-automatic tissue processor SE 400). Processed tissue samples were trimmed using a microtome (MR 2258-Histoline Laboratories semi-automatic microtome) and stained with haematoxylin-eosin (HE) for histopathological examination. Tissue samples were observed under an inverted microscope (OLYMPUS dual head microscope, CX43).

2.7 Statistical analysis

All data were reported as the Mean ± Standard deviation (SD). The statistical differences between groups and time points were identified by One-Way ANOVA ($p < 0.05$), and the interaction effects of groups and time points were determined by Two-Way ANOVA followed by Tukey as the post hoc test ($p < 0.05$) by using Minitab 16 statistical software (Minitab® 16.2.0, © 2010 Minitab Inc). The graphs and heatmaps were generated by Graphpad Prism 9.0 and Python software, respectively.

3. Results

3.1 Gross observations

Oral administrations to any tested groups did not lead to any mortality during the experimental period and there were no adverse signs and symptoms of toxicity. There were no considerable changes in animal behaviour during the time of the experiments. Furthermore, there were no statistically significant differences in body weight between the tested groups (Figure 2).

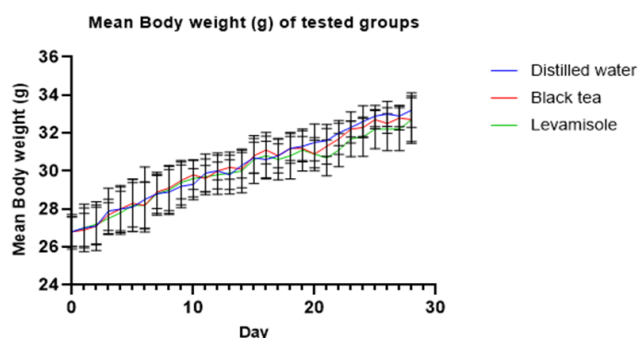


Figure 2. Mean body weight changes of animals studied in different experimental groups.

3.2 Immunoassay

The detectable expression levels were observed for GM-CSF, IL-2, IL- 4, IL-6, IL-12, MIP-1β, RANTES and TNF-α (Figure 3 a-h). The expression levels of IFN-γ and IL-10 were not quantified as they fell below the assay's minimum detectable range. GM-CSF, IL-4, IL-6, IL-12, RANTES and TNF- α are increased with the time point in the treatment group during the study period, while IL-2 and MIP-1β did not show such trends. The expression of RANTES in the treatment group is

significant compared to the negative control (Figure 3g) and GM-CSF (Figure 3a), IL- 4 (Figure 3c), IL-6 (Figure 3d), IL- 12 (Figure 3e) and TNF- α (Figure 3h) expressions were significantly expressed in positive control compared to the negative control group during the study ($p < 0.05$) (Figure 3).

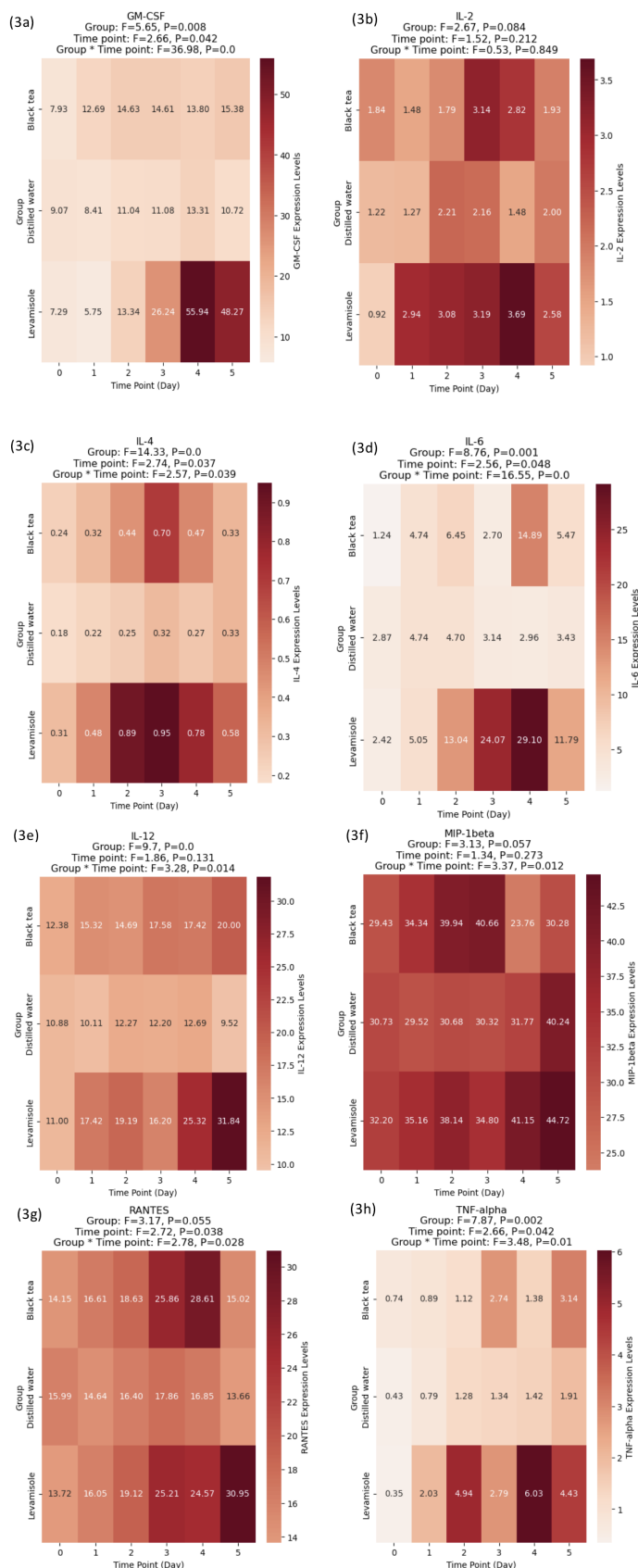


Figure 3. Cytokine profiles among the experimental groups (3a) GM-CSF, (3b) IL- 2, (3c) IL- 4, (3d) IL-6, (3e) IL- 12, (3f) MIP-1β, (3g) RANTES and (3h) TNF- α.

3.3 Histopathology

According to the histopathological examination, no significant treatment-related changes were observed in any of the experimental groups (Figure 4 a-o).

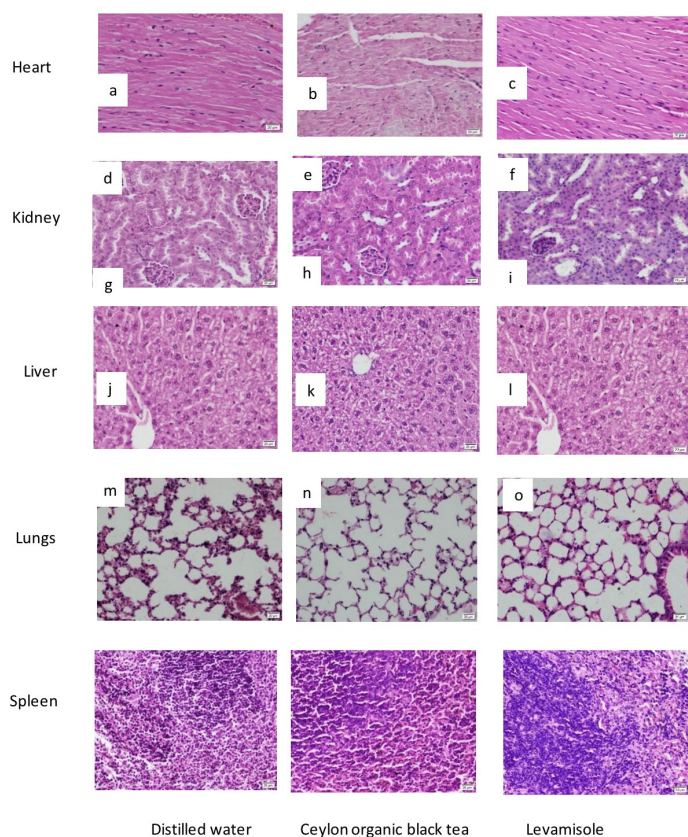


Figure 4. Typical histological structure of various organs (HE \times 200). Heart, kidney, liver, lungs and spleen in distilled water, Ceylon organic black tea and Levamisole-treated groups. No histological abnormalities were observed in any of the groups. Scale bars: 20 μ m.

4. Discussion

Boosting the immune system is crucial for overall well-being as it is the body's primary defence against various diseases. Therefore, a properly functioning immune system is essential for preventing infections, promoting recovery from illness, and maintaining overall health and well-being (Parkin and Cohen, 2001). Accurate assessment of immune function is crucial. Historically, medicinal plants have been utilised for their immune-enhancing properties (Chalamaiah *et al.*, 2014; Lin *et al.*, 2022).

Extensive research has been conducted to explore potential health benefits and identify the bioactive compounds responsible for these effects in tea. Compared to black tea, green tea has been the subject of numerous studies (Kuo *et al.*, 2014, Chowdhury and Barooah, 2020; Wang *et al.*, 2021). Previous research has highlighted the bioactive compounds in black tea, such as polyphenols, alkaloids, and amino acids, which

contribute to its health benefits. Black tea is rich in antioxidants and micronutrients, particularly beneficial for innate immune functions (Chowdhury and Barooah, 2020). This study used a mouse model to explore the relationship between black tea and selected cytokines and chemokines responsible for some pro-inflammatory and anti-inflammatory functions.

The previous findings have engaged with techniques like PCR to demonstrate upregulated mRNA levels of pro-inflammatory cytokines such as TNF- α and IL-6 following black tea polyphenol treatment, corroborating the findings of elevated protein levels in cytokine assays (Luo and Zheng, 2016). However, in contrast to previous findings, PCR determination of green tea has been shown to significantly upregulate IL-10 mRNA, an anti-inflammatory cytokine, in murine models, as reported by Sun *et al.* (2022). These findings underscore the unique immune-modulatory mechanism of black tea compared to other teas, with supporting and contrasting evidence from PCR and other techniques. Black tea modulation of Th2 responses, as indicated by elevated IL-4, is consistent with (Chowdhury and Barooah, 2020), who used ELISA and PCR to confirm cytokine shifts in BALB/c mice. Contrary to the previous finding, this study used a novel and robust design to direct quantification of cytokines in plasma following a treatment of Ceylon organic black tea in a mouse model, and this is the first study in which MILLIPLEX[®] MAP Mouse Cytokine/Chemokine Magnetic Bead Panel was deployed to assess the effect of tea in a mouse model. However, tea's antioxidant, anti-inflammatory, and gut microbiota-modulating effects are based on the multifactorial effect of the compositions that exist in the black tea and have not been sufficiently assessed in this study. Therefore, future research based on *in vivo* studies and clinical trials is needed to claim the benefits of black tea.

Changes in cytokines GM-CSF, IL-2, IL-4, IL-6, IL-12 (p70), TNF- α , MIP-1 β , 1 β and RANTES in the treatment group of the study indicate an immunomodulatory effect of Ceylon organic black tea. Further, this study revealed that Ceylon organic black tea does not cause cytokines to rise uncontrolled in the treatment group, which is harmful to the self-tissues and organs. Cytokines rarely act in isolation; they operate within complex, dynamic networks, engaging in synergistic, additive, or antagonistic interactions that fine-tune the immune response. Certain cytokines amplify each other's effects. For example, IFN- γ and IL-12 act synergistically to drive robust Th1 immune responses, enhancing cellular immunity critical for fighting intracellular pathogens (Trinchieri, 2003; Schroder *et al.*, 2004). Some cytokines counteract the effects of others.

IL-10, a potent anti-inflammatory cytokine, can inhibit the production and activity of TNF- α , IL-12, and IFN- γ , thereby helping to control excessive inflammation and prevent tissue damage (Moore *et al.*, 2001; Mosser and Zhang, 2008). Cytokines often trigger downstream cascades, amplifying the immune response. For instance, IL-6 can stimulate the production of secondary cytokines such as IL-10, TNF- α , and chemokines like MIP-1 β , leading to a broad and sustained inflammatory reaction (Tanaka *et al.*, 2014; Hunter and Jones, 2015). However, in this study IL-10 and MIP-1 β were not detected, though expression of IL-6 exists, leading to the expansion of similar future studies on more sensitive analysis of cytokines and extended study periods. Some cytokines establish positive feedback loops that perpetuate inflammation. GM-CSF, for example, promotes the activation and survival of macrophages, which secrete additional cytokines, further amplifying the inflammatory response (Hamilton, 2008; Shiomi and Usui, 2015).

This intricate interplay ensures that immune responses are appropriately scaled, but dysregulation of these networks can lead to pathological inflammation, autoimmune diseases, or cytokine storm syndromes (Merad and Martin, 2020). Therefore, the results observed for cytokine expression in Ceylon black tea indicate a more natural type of immunomodulation, despite the therapeutic immunostimulant used in the positive control group.

The safety profile of Ceylon organic black tea was confirmed through both behavioural observations and histopathological analysis. This study observed no significant changes in body weight, mortality, or adverse symptoms, with animals recovering quickly from initial mild weakness. Histopathological evaluations showed no pathological lesions in major organs, confirming the non-toxic nature of black tea. These results are consistent with previous studies using rodents (Sur *et al.*, 2015). The absence of vascular or inflammatory changes in the liver and normal kidney histoarchitecture indicates that black tea does not cause hepatic or renal toxicity. These observations reinforce the safety profile of Ceylon organic black tea, further supporting its use as a natural immunomodulatory agent.

In this study, the cytokine panel used was limited to selected targets, and further studies are needed to explore the modulation of a broader range of immune markers. This study demonstrated several encouraging findings. Notably, Ceylon organic black tea was confirmed to be safe, as evidenced by the absence of significant changes in body weight, mortality, or severe adverse symptoms in the subjects. The rapid recovery from an initial mild

weakness further underscores its tolerability. Histopathological examinations revealed no pathological lesions in major organs, supporting the conclusion that black tea does not induce hepatic or renal toxicity. Additionally, the lack of detectable levels of IFN- γ and IL-10 suggests the need for more sensitive assays to validate their potential roles. Future research should also focus on elucidating the molecular mechanisms underlying black tea-mediated immune modulation for long-term effects in different models to validate its health benefits and safety profile.

4. Conclusion

The findings of this study reveal the immunomodulatory potential of Ceylon organic black tea, demonstrating its ability to regulate key cytokine expression in a controlled and balanced manner. These effects are attributed to the bioactive molecules present in organic black tea, which support immune system function. Furthermore, the histopathological findings confirm that organic black tea, at the doses and duration tested, is safe for consumption, with no observed toxic effects or pathological changes in vital organs such as the liver and kidneys. These results highlight Ceylon organic black tea as a natural, safe immunomodulatory agent with potential health benefits. These findings highlight the value of Ceylon organic black tea, which provides a natural and accessible method for improving immune health and promoting overall well-being in people.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

The authors declare that financial support for the research and publication of this article was provided by English Tea Shop (UK) Ltd, 5th Floor, 3 Dorset Rise, London, EC4Y 8EN, United Kingdom.

References

- Abbas, A.K., Trotta, E. and Simeonov, D.R. (2018). Revisiting IL-2: Biology and therapeutic prospects. *Science Immunology*, 3(25), eaat1482. <https://doi.org/10.1126/sciimmunol.aat1482>
- Calder, P.C., Carr, A.C., Gombart, A.F. and Eggersdorfer, M. (2020). Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. *Nutrients*, 12(4), 1181. <https://doi.org/10.3390/nu12041181>

- Chalamaiah, M., Hemalatha, R., Jyothirmayi, T., Diwan, P.V, Kumar, P.U., Nimgulkar, C. and Kumar, B.D. (2014). Immunomodulatory effects of protein hydrolysates from Rohu (*Labeo rohita*) egg (roe) in BALB/c mice. *Food Research International*, 62, 1054-1061. <https://doi.org/10.1016/j.foodres.2014.05.050>
- Chattopadhyay, C., Chakrabarti, N., Chatterjee, M., Mukherjee, S., Sarkar, K. and Chaudhuri, A.R. (2012). Black tea (*Camellia sinensis*) decoction shows immunomodulatory properties on an experimental animal model and in human peripheral mononuclear cells. *Pharmacognosy Research*, 4(1), 15-21. <https://doi.org/10.4103/0974-8490.91029>
- Chowdhury, P. and Barooah, A.K. (2020). Tea Bioactive Modulate Innate Immunity: In Perception to COVID-19 Pandemic. *Frontiers in Immunology*, 11, 590716. <https://doi.org/10.3389/fimmu.2020.590716>
- Diehl, K.H., Vidal, Hull, R., Morton, D., Pfister, R., Rabemampianina, Y., Smith, D., Vidal, J.M. and Vorstenbosch, C.V.D. (2001). A Good Practice Guide to the Administration of Substances and Removal of Blood. *Journal of Applied Toxicology*, 21(1), 15-23. <https://doi.org/10.1002/jat.727>
- Dou, Q.P. (2019). Tea in health and disease. *Nutrients*, 11(4), 929. <http://doi.org/10.3390/nu11040929>
- Gholami, M., Rassouli, A., Mirzaei, S. and Hashemi, F. (2023). The potential immunomodulatory effect of levamisole in humans and farm animals. *Journal of Advanced Veterinary and Animal Research*, 10(4), 620. <http://doi.org/10.5455/javar.2023.j717>
- Hamilton, J.A. (2008). GM-CSF in inflammation and autoimmunity. *Trends in Immunology*, 29(10), 482-489. [http://doi.org/10.1016/s1471-4906\(02\)02260-3](http://doi.org/10.1016/s1471-4906(02)02260-3)
- Hunter, C.A. and Jones, S.A. (2015). IL-6 as a keystone cytokine in health and disease. *Nature Immunology*, 16(5), 448-457. <https://doi.org/10.1038/ni.3153>
- Kuo, C., Chen, T., Liou, S. and Hsieh, C. (2014). Immunomodulatory effects of EGCG fraction of green tea extract in innate and adaptive immunity via T regulatory cells in murine model. *Immunopharmacology and Immunotoxicology*, 36(5), 364-370. <https://doi.org/10.3109/08923973.2014.953637>
- Le Gros, G., Ben-Sasson, S.Z., Seder, R., Finkelman, F.D. and Paul, W. (1990). Generation of interleukin 4 (IL-4)-producing cells in vivo and in vitro: IL-2 and IL-4 are required for in vitro generation of IL-4-producing cells. *The Journal of Experimental Medicine*, 172(3), 921-929. <https://doi.org/10.1084/jem.172.3.921>
- Li, S., Lo, C.Y., Pan, M. H., Lai, C.S. and Ho, C.T. (2013). Black tea: chemical analysis and stability. *Food and Function*, 4(1), 10-18. <https://doi.org/10.1039/C2FO30093A>
- Lin, C., Chen, S., Lee, W. and Yen, G. (2022). Immunomodulatory effect of camellia oil (*Camellia oleifera* Abel.) on CD19 + B cells enrichment and IL-10 production in BALB/c mice. *Journal of Functional Foods*, 88, 104863. <https://doi.org/10.1016/j.jff.2021.104863>
- Luo, Y. and Zheng, S.G. (2016). Hall of fame among pro-inflammatory cytokines: interleukin-6 gene and its transcriptional regulation mechanisms. *Frontiers in Immunology*, 7, 604. <https://doi.org/10.3389/fimmu.2016.00604>
- Naveed, M., BiBi, J., Kamboh, A.A., Suheryani, I., Kakar, I., Fazlani, S. A., FangFang, X., Ali Kalhor, S., Yunjuan, L., Kakar, M.U., Abd El-Hack, M., Noreldin, A.E., Zhixiang, S., LiXia, C. and XiaoHui, Z. (2018). Pharmacological values and therapeutic properties of black tea (*Camellia sinensis*): A comprehensive overview. *Biomedicine and Pharmacotherapy*, 100, 521-531. <https://doi.org/10.1016/j.biopha.2018.02.048>
- Merad, M. and Martin, J.C. (2020). Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. *Nature Reviews Immunology*, 20(6), 355-362. <https://doi.org/10.1038/s41577-020-0331-4>
- Moore, K.W., de Waal Malefyt, R., Coffman, R.L. and O'Garra, A. (2001). Interleukin-10 and the interleukin-10 receptor. *Annual Review of Immunology*, 19(1), 683-765. <https://doi.org/10.1146/annurev.immunol.19.1.683>
- Mosser, D.M. and Zhang, X. (2008). Interleukin-10: new perspectives on an old cytokine. *Immunological Reviews*, 226, 205-218. <https://doi.org/10.1111/j.1600-065X.2008.00706.x>
- Murphy, K.M. and Weaver, C. (2017). Janeway's Immunobiology. 9th ed. New York, USA: Garland Science, Taylor and Francis Group, LLC.
- Parkin, J. and Cohen, B. (2001). An overview of the immune system. *Lancet*, 2, 357(9270), 1777-1789. [https://doi.org/10.1016/S0140-6736\(00\)04904-7](https://doi.org/10.1016/S0140-6736(00)04904-7)
- Preedy, V.R. (2013). Tea in Health and Disease Prevention. Amsterdam, The Netherlands: Elsevier Inc.
- Ridder, M. (2025). Tea market worldwide - statistics and facts. Retrieved from Statista website: <https://www.statista.com/topics/6922/tea-market-worldwide/#topicOverview>
- Sharma, V. and Rao, L.J.M. (2009). A thought on the

- biological activities of black tea. *Critical Reviews in Food Science and Nutrition*, 49(5), 379-404. <https://doi.org/10.1080/10408390802068066>
- Sharangi, A.B. (2009). Medicinal and therapeutic potentialities of tea (*Camellia sinensis* L.)—A review. *Food Research International*, 42(5-6), 529-535. <https://doi.org/10.1016/j.foodres.2009.01.007>
- Schroder, K., Hertzog, P.J., Ravasi, T. and Hume, D.A. (2004). Interferon- γ : an overview of signals, mechanisms and functions. *Journal of Leukocyte Biology*, 75(2), 163-189. <https://doi.org/10.1189/jlb.0603252>
- Shiomi, A. and Usui, T. (2015). Pivotal roles of GM-CSF in autoimmunity and inflammation. *Mediators of Inflammation*, 2015, 568543. <https://doi.org/10.1155/2015/568543>
- Sur, T.K., Chatterjee, S., Hazra, A.K., Mission, R., Educational, V. and Pradhan, R. (2015). Acute and sub-chronic oral toxicity study of black tea in rodents. *Indian Journal of Pharmacology*. <https://doi.org/10.4103/0253-7613.153423>
- Sun, J., Dong, S., Li, J. and Zhao, H. (2022). A comprehensive review on the effects of green tea and its components on the immune function. *Food Science and Human Wellness*, 11(5), 1143-1155. <https://doi.org/10.1016/j.fshw.2022.04.008>
- Suzuki, T., Miyoshi, N., Hayakawa, S., Imai, S., Isemura, M. and Nakamura, Y. (2016). Health benefits of tea consumption. In Wilson, T. and Temple, N.J. (Eds.). *Beverage Impacts on Health and Nutrition*. 2nd ed, p. 49-67. New York, USA: Humana Press. https://doi.org/10.1007/978-3-319-23672-8_4
- Tanaka, T., Narazaki, M. and Kishimoto, T. (2014). IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology*, 6(10), a016295. <https://doi.org/10.1101/cshperspect.a016295>
- Tang, G.Y., Meng, X., Gan, R.Y., Zhao, C.N., Liu, Q., Feng, Y.B., Li, S., Wei, X.L., Atanasov, A.G., Corke, H. and Li, H.B. (2019). Health functions and related molecular mechanisms of tea components: an update review. *International Journal of Molecular Sciences*, 20(24), 6196. <https://doi.org/10.3390/ijms20246196>
- Trinchieri, G. (2003). Interleukin- 12 and the regulation of innate resistance and adaptive immunity. *Nature Reviews Immunology*, 3(2), 133-146. <https://doi.org/10.1038/nri1001>
- Von Luetichau, I., Nelson, P.J., Pattison, J.M., Van De Rijn, M., Huie, P., Warnke, R., Wiedermann, C.J., Stahl, R.A.K., Sibley, R.K. and Krensky, A.M. (1996). RANTES chemokine expression in diseased and normal human tissues. *Cytokine*, 8(1), 89-98. <https://doi.org/10.1006/cyto.1996.0012>
- Wang, S., Li, Z., Ma, Y., Liu, Y., Lin, C.C., Li, S., Zhan, J. and Ho, C.T. (2021). Immunomodulatory effects of green tea polyphenols. *Molecules*, 26(12), 3755.
- Yilmaz, Y. (2025). Health-Promoting Effects of Black Tea: A Narrative Review of Clinical Trials. *International Journal of Food Science*, 1, 8560718. <https://doi.org/10.1155/ijfo/8560718>
- Zhang, Y., Larsson, S.C., Huang, X., Zhuang, P. and Chen, L. (2022). Tea consumption and all-cause and cause-specific mortality in the UK Biobank: A prospective cohort study. *Annals of Internal Medicine*, 175(9), 1201-1211. <https://doi.org/10.7326/M22-0726>