Heliyon

CellPress

Heliyon editors

Heliyon is actively building individual sections that are managed by respected researchers and experts in the field. These dedicated and experienced section editors and their teams of associate editors, supported by our in-house editorial team, are responsible for managing the peer review process for all submitted manuscripts within their subject sections. These dedicated sections allow us to tailor each author's experience to the needs and standards they have come to expect within their respective fields. See editorial board vacancies here.

Heliyon has recently created a collection of publications from our editorial board, which you may be interested in reading.

Agriculture

Meet the full editorial team for ***Heliyon Agriculture***.

Prof. Athanasios Damialis

Dr. Athanasios Damialis is a multi-disciplinary scientist working for more than 20 years on the fields of plant and fungal ecology, environmental sciences, biometeorology, climate change and environmental health. His particular focus lies on the reproductive biology of plants (flowering phenology, atmospheric circulation of airborne pollen) and on endophytic fungi. He uses an inter-disciplinary research approach with environment-environment interactions and human-environment interactions. This includes mainly those interactions including, but not limited to, the detection of bio-climatic indicators and spatiotemporal patterns of plant, forest and agricultural habitats and ecosystems, in relation to ongoing and simulated climate change. His research goal is to comprehend the responsive ability of organisms under stress conditions, ultimately, attempting to promote sustainable growth and environmental quality.

Biochemistry, molecular biology and cell biology

Meet the full editorial team for ***Heliyon Biochemistry, molecular biology and cell biology***.

Prof. Nicola Zambrano

Nicola Zambrano is professor of Molecular Biology at the University of Naples Federico II, and group leader at CEINGE Advanced Biotechnologies, Naples, Italy. He holds a M.Sc. degree in biological sciences and a Ph.D. in biotechnologies, acquired within a joint doctoral program from the Universities of L'Aquila and Naples, Italy. He was a visiting fellow at National Cancer Institute, NIH in Bethesda from 1991 to 1994, and visiting scientist at EMBL in Heidelberg, Germany in 1997. His academic career at the Federico II University in Naples started with an assistant professor position in biochemistry (1996), before being enrolled as an associate professor (2002) and then, as a full professor in molecular biology (2010).

Prof. Jinrong Min

Professor Jinrong Min received his Ph.D. degree in physics from the Institute of Physics, Chinese Academy of Sciences in China, and carried out his post-doctoral training in chromatin structural biology at the Cold Spring Harbor Laboratory, USA. He is currently the principal investigator of the Chromatin Structural Biology Group at the Structural Genomics Consortium (SGC), University of Toronto, and an associate professor in the Department of Physiology at the University of Toronto.

Biology

Meet the editorial team for ***Heliyon Biology***.

Prof. Yu-Chung Chiang

Research piloted in my research answers a key biological question: how do genetic signals within and among species reveal evolutionary and geographical structure, including plant phylogeography of East Asia and the Pacific Islands, introgression between wild populations and cultivars, and conservation genetics on rare and endemic plant.

Business and economics

Meet the full editorial team for ***Heliyon Business and economics***.

Dr. Larisa Yarovaya

Doctor Larisa Yarovaya received her doctorate in finance from Northumbria University in England. Currently, she is a lecturer in finance, Programme Director BSc Finance, and deputy head of Centre for Digital Finance at the Southampton Business School, University of Southampton.

Dr. Yarovaya is a researcher the fields of international finance, digital finance, financial integration, Islamic finance, energy economics, information transmission, and international business. She has published her research in peer-reviewed academic journals and is an associate editor of the *International Review of Financial Analysis, Journal of International Financial Markets Institutions and Money, Heliyon*, and *Data-in-Brief*.

Assoc. Prof. Pavlos Delias

Pavlos Delias is a tenured faculty member at the International Hellenic University, Department of Accounting and Finance. He holds a jointly supervised PhD from both Technical University of Crete and University Paris Dauphine, under a cotutelle agreement.

Pavlos Delias has been invited as a visiting professor in several universities (national as well as international). He has contributed to numerous research projects, focusing on applying the principles of business analytics and operational research to decision support systems design and use. He is also a member of the coordination board for the EURO working group on decision support systems. His research interests are in the areas of business process analytics, business analytics and operational research, and multiple criteria analysis.

Assoc. Prof. Eugene Ezebilo, PhD

Eugene Ezebilo is an Associate Professor of Economics. He received his PhD in Economics from Swedish University of Agricultural Sciences, Sweden. He is currently a Deputy Director for Research at the National Research Institute, Port Moresby in Papua New Guinea. He is a guest lecturer at University of Papua New Guinea where he teaches two courses in the Master of Economics and Public Policy program. In the past ten years, Eugene's research has focused primarily on the economic value of ecosystem goods and services, land use planning, affordable housing and economic development. His academic career started at Swedish University of Agricultural Sciences as a Post-Doctoral Researcher in Environmental and Natural Resource Economics, followed by an Assistant Professor in Economics and Planning from the same university, where he later became an Associate Professor of Economics. His research interests are in environmental and resource economics, housing economics and policy, land use planning and economic development.

Cancer Research

Meet the full editorial team for ***Heliyon Cancer Research***.

Prof. Graham Pawelec

Graham Pawelec received an MA in Natural Sciences and a PhD in Transplantation Immunology from the University of Cambridge, UK. He is currently Professor of Experimental Immunology in the Department of Immunology, University of Tübingen, Tübingen, Germany. He is a Visiting Professor at Nottingham Trent University, UK and at King´s College London, UK, holds an Honorary Chair at Manchester University, UK. He is a member of the Cancer Solutions Program at the Health Sciences North Research Institute of Canada, Sudbury, Ontario, Canada. He is currently Co-Editor-in-Chief of "Immunity and Aging". Graham's research interests are centred on alterations to immunity, especially T cell-mediated immunity, in ageing and cancer in man, and the influence these have on the outcome of vaccination and immunomodulatory antibody therapies. The impact of polypathogenicity (including multiple infections, cancer, Alzheimer´s, diabetes, autoimmunity) as well as stress (psychological, nutritional) on immune signatures reflecting individual immune status is of particular interest in the clinical context.

Dr. Kamal Kant Sahu

Dr. Kamal Kant Sahu is a fellow in hematology and medical oncology at the Huntsman Cancer Institute at the University of Utah in Salt Lake City. Dr. Sahu received his medical education at the Chhattisgarh Institute of Medical Sciences in Bilaspur, India. He completed training in internal medicine and subsequently a fellowship in clinical hematology and bone marrow transplantation at the Postgraduate Institute of Medical Education and Research (PGIMER) in Chandigarh, India. After coming to the United States, Dr. Sahu undertook residency training in internal medicine at Saint Vincent Hospital in Worcester, Massachusetts, and, in July 2021, began his fellowship training in hematology and medical oncology at the Huntsman Cancer Institute. Dr. Sahu is active in clinical research and has published widely with over 200 papers in PubMed-indexed journals. His clinical and research interests focus on genitourinary malignancies.

Chemical Engineering

Meet the full editorial team for ***Heliyon Chemical Engineering***.

Prof. Bart Van der Bruggen

Bart Van der Bruggen received his PhD in chemical engineering from KU Leuven in 2000. He currently works as full professor at KU Leuven (Belgium) and extraordinary professor at Tshwane University of Technology (South Africa). He has vast experience as an editor for various journals and is a also very active author and reviewer, with over 600 publications, cited more than 25,000 times. His expertise is in separation processes in classical and non-classical chemical engineering applications, with a focus on membrane science and technology.

Chemistry

Meet the full editorial team for ***Heliyon Chemistry***.

Dr. Francesco Epifano

Prof. Epifano obtained his degree in medicinal chemistry and pharmaceutical technology in 1993 from the University of Perugia, Italy. In 1998, he obtained his Ph.D. in agricultural entomology at the Faculty of Agricultural Sciences of the University of Perugia. Currently, he is an associate professor of medicinal chemistry at the Department of Pharmacy of the University Gabriele D'Annunzio of Chieti-Pescara. His recent work is concerned with synthesis and pharmacological properties of secondary metabolites from plants, fungi, and bacteria. Dr. Epifano was the recipient of the 2010 IADR / Glaxo Smith Kline Innovation in Oral Care Award as the co-investigator of the project entitled “Therapeutic potential of Citrus auraptene for periodontal disease”, the 2012 Apivita Award for Phytochemistry, and the 2017 Pierre Fabre – Phytochemical Society of Europe Innovation Award.

Clinical research

Meet the full editorial team for ***Heliyon Clinical research***.

Dr. Carolyn Mackintosh-Franklin

Dr. Carolyn Mackintosh-Franklin has had an extensive career in both clinical practice and higher education working at the University of Bradford, University of Liverpool, University of Hull and currently working at the University of Manchester. She received her first degree from the University of Newcastle Upon Tyne, her MSc from the University of Manchester and doctorate from the University of Bradford. She is also a registered nurse specializing in the assessment and management of acute and chronic pain. Her research interests are broad ranging; encompassing work on health care professionals' attitudes towards those in pain, aspects of pain assessment and management, and pedagogic research into learning needs of mature students, with a range of highly cited publications and conference presentations in these areas.

Dr. Avril Mansfield, R.Kin, PhD

Avril Mansfield received a BSc in Sport and Exercise Science and MSc in Biomedical Engineering from the University of Limerick, Ireland, and PhD in Medical Science from the University of Toronto, Canada. She is also a Registered Kinesiologist. She is appointed as a Senior Scientist at KITE-Toronto Rehabilitation Institute, University Health Network, and is cross appointed as an Associate Professor in the Department of Physical Therapy at the University of Toronto, and Affiliate Scientist with the Hurvitz Brain Sciences Program, Evaluative Clinical Sciences, Sunnybrook Research Institute. Her research aims to improve safe independent mobility among older adults and people with neurological injury and disease by improving balance control, reducing falls and injury risk, and increasing participation in exercise and physical activity. Her work spans basic research in motor control and motor learning, clinical trials, and implementation.

Prof. Giuseppe Musumeci

Giuseppe Musumeci received a BSc, MSc and PhD in Sport and Exercise Science from the University of Catania, Italy. Currently, he works as a Full Professor of Sport and Exercise Science at the Department of Biomedical and Biotechnological Sciences, School of Medicine, University of Catania, Italy. He is also an Adjunct Professor at the Faculty of Sport Sciences, Fujian Normal University, Fuzhou, China. Prof. Musumeci is the Director of the Research Center on Motor Activities (CRAM), the Director of the School of Posturology and Physical Exercise Sciences, the Dean of the Human Movement Sciences Faculty and the Head of the Movement Innovation PosturaLab at the University of Catania. Musumeci's research interests are centred on preventive and adapted physical activity for all chronic non-communicable diseases and kinesitherapy and posturometric activity for the main paramorphism and dysmorphisms of our body. Other research topics of interest are osteoarthritis and musculoskeletal disorders and the relative effects of diet, ageing and physical activity.

Computer science

Meet the full editorial team for ***Heliyon Computer science***.

Assoc. Prof. Jonathan Chan

Assoc. Prof. Jonathan H. Chan is an associate professor of computer science and a co-founder of D-Lab at the School of Information Technology, King Mongkut's University of Technology Thonburi, Thailand. Jonathan holds a Ph.D. from the University of Toronto, where he has also served as a visiting professor. In addition to his role as the section editor of *Heliyon Computer science*, Dr. Chan is an action editor of *Neural Networks*, and a member of the editorial boards of *International Journal of Machine Intelligence and Sensory Signal Processing*, *International Journal of Swarm Intelligence*, and *Proceedings in Adaptation, Learning and Optimization*.

Dr. Chan is a founding member and a current VP of the IEEE-CIS Thailand Chapter, and a senior member of IEEE, ACM, and INNS, a member of the Professional Engineers of Ontario (PEO), and a governing board member of APNNS. He also holds an NVIDIA Deep Learning Institute (DLI) University Ambassadorship and is a certified DLI instructor. His research interests include intelligent systems, biomedical informatics, and data science and machine learning in general.

Dentistry

Meet the full editorial team for ***Heliyon Dentistry***.

Gaetano Isola, PhD

Dr. Gaetano Isola qualified in Dentistry at the University of Messina, Italy and obtained his PhD in “Physiopathology of the Stomatognatic Apparatus and Dental Materials” at the University of Turin, Italy. He is a visiting research fellow at the Laboratory of the Study of Calcified Tissues and Biomaterials at the Department of Periodontology, Université de Montréal, Canada. Dr. Isola did an advanced course in periodontology at the University of Ferrara and a 3-year certificate in oral surgery at the University of Naples “Federico II.” He is a visiting Professor at the Department of Periodontology, University of North Carolina at Chapel Hill, USA and at the Department of Oral Surgery, University of Granada, Spain. He is also a visiting researcher at the Department of Implantology and Oral Surgery, University of Bern, Switzerland, and the Department of Periodontology, Eastman Dental Institute, London.

Dr. Isola is an active member of the Italian Society of Oral Surgery (SIdCO) and of the International Piezoelectric Surgery Academy (IPA). He serves on the board of the International Association of Dental Research (IADR) and is a member of the Italian Society of Periodontology (SIdP), as well as an active member of the International IADR Constitution Committee of the International Association of Dental Research (IADR) (2016–2019 and 2019–2022).

His main research interests focus on the clinical, biological, and pharmacological aspects of periodontitis, and the relationship between oral health and systemic health and the pre-neoplastic disorders.

Earth science

Meet the full editorial team for ***Heliyon Earth science***.

Prof. Andrew S. Hursthouse

Professor Hursthouse is a professor of environmental geochemistry at the University of the West of Scotland (UWS) and holds a Ph.D. in environmental radioactivity from University of Glasgow and a B.Sc. degree in geochemistry from University of Reading. He holds a 100 talent high-end expert fellowship at Hunan University of Science & Technology, Xiangtan, PRC. He has editorial roles in several earth and environmental science journals and has worked in academic and industrial research environments.

Professor Hursthouse's areas of interest and expertise are in earth process interactions and the environmental geochemistry of metallic elements, resource exploitation and implications for human health, and this approach also applied to environmental pollution, industrial processes, economic development and society; remediation and treatment of chemical pollution; chemical and environmental hazards, waste and environmental management and regulation.

Education

Meet the full editorial team for ***Heliyon Education***.

Prof. David González-Gómez

Heliyon Education is led by Section Editor David González-Gómez, Ph.D. Dr. González-Gómez is a Professor in the Department of Science and Mathematics Education and the Dean of the Teaching Trainer School at the University of Extremadura (Spain). Dr. González-Gómez is known internationally for work in science education; science, technology, engineering, and mathematics (STEM); active learning methodologies for teaching science; affective domain in the science learning process; education for the sustainability; SDGs. Currently, he is an advisory council of the Science, Technology, and Innovation of Extremadura government in Spain.

Energy

Meet the full editorial team for ***Heliyon Energy***.

Dr. Socrates Kaplanis

Prof. Socrates Kaplanis obtained his degree in physics from University Thessaloniki, a MSc in nuclear reactors from Aston University, and a PhD in radiation detection and modelling from the University Patra. He has held academic positions including professor of renewable energy systems at the Technological Educational Institute of Patra, head of the renewable energy systems laboratory, honorary professor and doctor honoris causa at the Transylvania University in Brasov, and as a visiting professor at the University of Applied Sciences in Aachen, Germany.

Prof. Kaplanis has a research background in solar radiation, prediction modelling, zero and intelligent energy buildings, PV systems engineering, solar thermal engineering, and PV based hybrid systems. He has held various posts, including

president of the Technological Educational Institute of Patra, president of the Technological Educational Institute of Western Greece, and vice-president and President of the European Institutions in Higher Education (EURASHE).

Engineering

Meet the full editorial team for ***Heliyon Engineering***.

Prof. Andrea Francesco Morabito

Professor Andrea Francesco Morabito received his Ph.D. in computer, biomedical, and telecommunications engineering from the University of Reggio Calabria, Italy, where he has also served as an assistant professor in electromagnetic fields since 2010. His research work is mainly focused on models and effective strategies for the solution of inverse problems, in particular, antenna synthesis, phase retrieval, and electromagnetic inverse scattering.

Prof. Mohammad Mehdi Rashidi

Professor Mohammad Mehdi Rashidi received his Ph.D. in mechanical engineering from Tarbiat Modares University, Iran. He is currently a professor of mechanical engineering at Tongji University in Shanghai, China, and previously taught at Bu-Ali University in Iran. Prof. Rashidi was named a 2018 highly cited researcher by Clarivate Analytics.

Environment

Meet the full editorial team for ***Heliyon Environment***.

Prof. Frederic Coulon

Professor Frederic Coulon holds a chair in Environmental Chemistry & Microbiology at Cranfield University, UK. In addition to his position as section editor for *Heliyon Environment*, Prof. Coulon is an associate editor for *Environment International* and *Science of the Total Environment*. His professional interests include: soil and water chemistry; fate and transport of chemicals in surface and subsurface waters; water and wastewater treatment; soil and sediment treatment; hazardous waste site remediation; energy and environment; population and environment; and public communication of environmental science and engineering. His research achievements address international priorities under the umbrella of the Water-Soil-Waste nexus across sectors and scales. His work is premised on the understanding that environmental resources are inextricably intertwined and therefore there is a need of advancing a nexus approach to enable integrated and sustainable management of water, soil and waste systems.

Prof. Christian Sonne

Professor Christian Sonne, DVM, PhD, DScVetMed, Dipl. ECZM-EBVS, holds a professorship in veterinary ecotoxicology and wildlife medicine at Aarhaus University, Denmark. In addition to his position as section editor for *Heliyon Environment*, Prof. Sonne serves as special issues editor for *Environmental Pollution*. Since 1997, Prof. Sonne has specialized in the cross-field of biological effects from exposure to environmental chemicals, diseases and climate change, giving him a unique insight and profile working with a broad range of animals including predatory mammals, raptorial birds, sea birds, fish and humans. He has a broad insight and interest in internal and reproductive organs (histopathology, size, and morphology), skeletal system (bone density and morphology using e.g. DXA scanning), immune system (intra dermal testing of lymphocyte functioning, immune globulin production and cytokine and APP expressions), endocrine system (steroid and peptide hormones), PBPK modelling, blood biochemistry and infectious diseases (zoonosis). Prof. Sonne uses his global network to obtain interdisciplinary research results. Since 2015, he has applied his in-depth knowledge and understanding of biological processes to also include specific un-solved wildlife issues in Denmark (eider duck population declines) and health of raptors. Recently his innovative approaches have led to the first interactions with private industry focusing on natural resources developments and translational medicine within insulation, osteoporosis and metabolic syndrome. Prof. Sonne also specializes in surgical field implantations of intra-coelomic (abdominally) and subcutaneously satellite transmitters (PTTs) in various sea bird species and immobilization of deer spp.

Food science and nutrition

Meet the full editorial team for ***Heliyon Food science and nutrition***.

Dr. Lilian Mariutti

Dr. Lilian R. B. Mariutti received her aaster and doctorate degrees in food science from the School of Food Engineering - University of Campinas, Brazil, where she currently has a position as assistant professor. She was a researcher fellow in the Laboratory of Veterinary Drug Residues of the Brazilian Ministry of Agriculture, Livestock and Food Supply. Her research focuses on the identification and bioaccessibility of bioactive compounds and lipids and design of food ingredients from non-conventional sources.

Genetics

Meet the full editorial team for ***Heliyon Genetics***.

Qiang Wu, PhD

Dr. Qiang Wu is an associate professor in the State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology. He obtained his Ph.D degree from National University of Singapore in 2003. He then received his postdoc training in Genome Institute of Singapore (Mentor: Prof Huck Hui Ng) and the Gurdon Institute, University of Cambridge (mentor: Prof Magdalena Zernicka-Goetz). He went back to National University of Singapore as

an assistant professor in 2009. He joined Macau University of Science and Technology in 2017.

Dr. Wu's research interest is to study how genetic and epigenetic factors determine stem cell fates and regulate cancer progression with a combination of molecular, cellular and high throughput approaches.

Global Health & Infectious Diseases

Meet the full editorial team for ***Heliyon Global Health & Infectious Diseases***.

Dr. Chaisiri Angkurawaranon
Public Health
Chiang Mai University, Chiang Mai, Thailand

Chaisiri Angkurawaranon received his MD from Chiang Mai University and specialises in Family Medicine. He received a Masters in Medical Statistics and a PhD in Non-communicable Disease Epidemiology from the London School of Hygiene and Tropical Medicine. His research focuses on global health issues related to ageing and chronic conditions (both communicable and non-communicable) in primary care.

Prof. Keertan Dheda, PhD
Infectious Disease
London School of Hygiene & Tropical Medicine, London, United Kingdom

Professor Keertan Dheda is a hospital-based general physician, pulmonologist, and a critical care specialist who heads up the Division of Pulmonology at Groote Schuur Hospital and the University of Cape Town. He is a South African National Research Foundation 'A'-rated clinician scientist and has professorial appointments at the University of Cape Town and the London School of Hygiene and Tropical Medicine. He serves on several national and international academic and advisory bodies, including the editorial boards of the American Journal of Respiratory and Critical Care Medicine and Lancet Respiratory Medicine.

Assoc. Prof. Nitika Pant Pai
Infectious Disease
McGill University, Montreal, Canada

Dr. Nitika Pant Pai is a tenured Associate Professor in the Department of Medicine at McGill University. Her global implementation research program for the past twenty years is focused on point-of-care diagnostics for HIV and other sexually transmitted blood borne infections; specifically the innovation, implementation and impact of digital strategies with rapid diagnostics and wearable solution. She develops integrated connected strategies with digital innovations, Bayesian diagnostics, artificial intelligence to plug health service delivery gaps in diagnostics in rapid diagnostics. She serves to inform domestic and global policy on point-of-care diagnostics.

Her research program is based in Canada, India and South Africa. She has led many diagnostic trials, cohort/cross sectional studies, meta-analyses, systematic reviews, modelling studies, to inform the gaps in policies to end the HIV epidemic. Her research has been supported by grants from the Canadian Institutes of Health Research, the FRQS, Grand Challenges Canada, Bill and Melinda Gates Foundation, National Institutes of Health, MRC SHIP, South African DST, IC-IMPACTS, Clinton Health Access Initiative, among others.

She has served on many technical working groups for national and international agencies: WHO, Foundation for Innovative Diagnostics, PSI, The Bill and Melinda Gates Foundation, ASLM, CDC, PHAC, REACH, among others. She has advised the office of the US Congress on multiplex testing. She has also contributed to HIV self-testing guidelines and policy guidance for HIV self-testing for the WHO. She serves the Strategic Advisory Board of the Foundation for Innovative Diagnostics and is on WHO's Roster of Digital Health Experts. She serves on the Editorial Moard for biomedical journals and regularly reviews for key international health agencies.

She is an elected member of the College of New Scholars, Artists & Scientists of the Royal Society of Canada.

Dr. Marcos Roberto Tovani-Palone

Marcos Roberto Tovani Palone completed his MSc from the Hospital for Rehabilitation of Craniofacial Anomalies, University of São Paulo, Brazil, and PhD in Experimental Pathology from Ribeirão Preto Medical School, University of São Paulo, Brazil. He is a DDS specializing in different fields of health, including pediatric dentistry, syndromes and craniofacial anomalies, health management, and health surveillance. He has published more than 100 papers in reputed journals and has been serving as an editorial board member of important biomedical journals. His main research interests focus on pediatric pathology, orofacial clefts, general medicine, dentistry, global and public health. More recently in 2021, he obtained the degree of Public Administration. With an ongoing involvement in many projects and high impact research activities, he has established important international collaborations with researchers from all over the world.

Immunology

Meet the full editorial team for ***Heliyon Immunology***.

Mats Waldemar Johansson, PhD
Immunology, Eosinophils
Dr. Mats W. Johansson received his PhD degree in biology within the research field of invertebrate immunology/innate immunity at Uppsala University, Sweden, was a postdoctoral fellow in cell biology at the Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California, USA, and was then an Assistant and Associate Professor, and Director of Studies of biology at Uppsala University. He is currently a Senior Scientist and Research Professor (honorific) at the Morgridge Institute for Research, Madison, Wisconsin, USA, and affiliated as an Honorary Associate/Fellow with the Division of Allergy, Pulmonary and Critical Care Medicine of the Department of Medicine and the Department of Biomolecular Medicine, University of Wisconsin-Madison. Since coming to Madison he has done research on eosinophil biology, asthma, and eosinophilic esophagitis (EoE), and now recently also COVID-19.

Information Science

Meet the full editorial team for ***Heliyon Information Science***.

Prof. Gregorio González Alcaide

Gregorio González-Alcaide (PhD) is a full Professor at the Department of the History of Science and Library & Information Sciences, at the University of Valencia.

Dr. González Alcaide teaching activities include Bibliometrics, skills in writing and academic communication and processes for evaluating research activities. He has also worked to raise awareness on the importance of academic honesty, to discourage behaviors like plagiarism and to foster respect for the ethical principles that must guide the research and publication process.

His main line of research has focused on the study of scientific collaboration by means of Bibliometrics and social network analysis as research methodologies. His studies have aimed to determine the extent of cooperative practices, structural properties, and the characteristics of scientific networks at different analytical levels (authors, institutions, and countries) and in different disciplines or areas of knowledge. He has also investigated cooperative practices as a process and researchers' perceptions with regard to this phenomenon, combining quantitative and qualitative approaches based on surveys and interviews.

Materials science

Meet the full editorial team for ***Heliyon Materials science***.

Prof. Luis M. Gandía

Luis M. Gandía is a full professor of chemical engineering at the Public University of Navarre (UPNA) since 2010. Prof. Gandía obtained his Ph.D. in chemistry at the Faculty of Chemistry of the University of the Basque Country in Donostia/San Sebastián in 1993. He is a founding member of the Institute for Advanced Materials (InaMat) at UPNA. He is the head of a multi-disciplinary research team mainly working on renewable resources valorization and the development of catalytic materials for environmental and energy applications. His research interests include: preparation and physico-chemical characterization of heterogeneous catalysts; structured and micro-structured catalysts and chemical reactors; photocatalysis; biofuels and synthetic fuels; hydrogen energy; Li-ion batteries; methane conversion; CO_2 valorization and Computational Fluid Dynamics (CFD).

Mathematics

Meet the full editorial team for ***Heliyon Mathematics***.

Prof. Hermann J. Eberl

Dr. Hermann Eberl is a professor in the Department of Mathematics and Statistics at the University of Guelph (Canada), where he is also the director of the Biophysics Interdepartmental Graduate Program. Prior to joining the University of

Guelph he obtained his graduate degrees (Dipl.Math., Dr.rer.nat) at the Technical University of Munich (Germany) and was a postdoctoral fellow first at the Delft University of Technology (the Netherlands), and then at the GSF National Research Center for Environment and Health in Oberschleissheim (Germany).

His research is in mathematical modelling, analysis, and simulation of biological systems and their interaction with their physical environment. This encompasses dynamical systems, partial differential equations, numerical analysis and scientific computing. The two primary strands of his research in recent years were the development and application of mathematical methods in biofilm research and mathematical modelling of honeybee colonies and their diseases.

Assoc. Prof. Yilun Shang, PhD

Dr. Yilun Shang is an Associate Professor in the Department of Computer and Information Sciences at Northumbria University (UK), where he is also the Program Lead of MSc Artificial Intelligence. Prior to joining Northumbria, he obtained his BS and PhD degrees in Mathematics from Shanghai Jiao Tong University (China) and was an Associate Professor of Mathematics in Tongji University (China).

His research interests mainly include complex networks, nonlinear dynamics, applied probability, combinatorics, algorithms, and computation. Some primary strands of his research in recent years were the topological indices of graphs, network resilience, random graphs, and distributed cooperative control of multiagent systems.

Microbiology

Meet the full editorial team for ***Heliyon Microbiology***.

Assoc. Prof. Dana Stanley

Associate Professor Dana Stanley was awarded a PhD in molecular microbiology from Victoria University, Melbourne, in 2009. Her PhD project, “Generation and Characterisation of Ethanol-Tolerant Saccharomyces cerevisiae Mutants,” investigated the molecular and metabolic determinants of ethanol tolerance in yeast and was awarded “the most outstanding PhD in 2009” by the University. Prof. Stanley held a postdoctoral position in CSIRO’s Animal Health Laboratories (AAHL), one of the world’s most sophisticated animal research laboratories, where she researched poultry intestinal health, specifically gut microbiota and genetics. Currently, Prof. Stanley is a leader of the molecular microbiology research cluster at Central Queensland University, focusing in human and livestock intestinal health, probiotic and next generation antibiotic development and pathogen control. She is working in collaboration with world’s leading probiotic companies on research projects aiming to improve intestinal health of agricultural animals and humans. Prof. Stanley’s work has been published in *Nature Medicine* (as the first author), *Nature Communications* and *Nature Immunology*.

Neuroscience

Meet the full editorial team for ***Heliyon Neuroscience***.

Assoc. Prof. Mario Tiberi

Dr. Mario Tiberi is a senior scientist at the Ottawa Hospital Research Institute's Neuroscience Program, and associate professor at the University of Ottawa Faculty of Medicine in the departments of medicine, cellular and molecular medicine, and psychiatry. He is also a member of the University of Ottawa Brain and Mind Research Institute. Dr. Tiberi completed his PhD in Pharmacology (1990) on opioid receptors at the Université de Montréal under the supervision of Dr. Jacques Magnan, before moving on to a very successful post-doctoral training at the Howard Hughes Medical Institutes at Duke University in Dr. Marc Caron's laboratory. It was during his postdoctoral training that Dr. Tiberi refined his area of research expertise in molecular biology and biochemistry of dopamine receptors. His research interests focus on dopamine receptors, G proteins, signal transduction, desensitization and phosphorylation. Dr. Tiberi's work aims to understand complex structure and molecular relationships of dopamine receptor signaling complexes using in vitro cellular systems and pre-clinical in vivo models, with the aim of aiding in the development of novel therapeutic strategies for brain disorders such as Parkinson's disease, stroke, schizophrenia and drug addiction. Dr. Tiberi has published over 50 scientific papers and edited two books. He has wide experience with undergrad and graduate student supervision as well as teaching. Many of his former graduate students have gone on to successful independent research careers.

Pharmaceutical science, pharmacology and toxicology

Meet the full editorial team for ***Heliyon Pharmaceutical science, pharmacology and toxicology***.

Prof. Emilio Clementi

Emilio Clementi graduated in medicine and surgery at the University of Milano, received his doctorate in pharmacotherapy at the University of Brescia to move as research fellow to the University College London. He is currently full professor of pharmacology and director of the clinical pharmacology unit of the National Health System at the University of Milano, co-opted member in the executive committee of the International Union of basic and clinical Pharmacology (IUPHAR).

He has published on the pathophysiology of nitric oxide and its relevance in therapeutic perspective, especially in skeletal muscle, and on pharmacokinetics, pharmacogenetics and pharmacoepidemiology in paediatry. He is presently the editor in chief of pharmacological research.

Prof. Dimitrio Lamprou

Dimitrios Lamprou (Ph.D. MBA) is a reader in pharmaceutical engineering and the MSc programme director in industrial pharmaceutics at the School of Pharmacy in Queen's University Belfast (UK). He is also the chair at United Kingdom and Ireland Controlled Release Society (UKICRS). Dr. Lamprou specialises in the areas of pharmaceutical manufacturing & emerging technologies and his research and academic leadership have been recognised in a range of awards, including the Royal Pharmaceutical Society Science Award and the Scottish Universities Life Sciences Alliance Leaders Scheme Award. His group is applying nano and microfabrication techniques in pharmaceutical and medical device manufacturing, such as 3D printing & bioprinting, electrospinning and microfluidics.

Dr. Martin Leonard

Dr. Leonard obtained his PhD in pharmacology in 2000 from University College Dublin, Ireland. He has over 15 years' experience as a toxicologist focussed to developing and improving on models and methods for assessment of toxicological hazard, including the use of high content omics technology and iPSC in vitro models of the airway. Dr. Leonard is a European registered toxicologist and currently holds a position as principal toxicologist at Public Health England directing research into the mechanisms of allergen and particulate hazard associated with asthma and allergic airway disease. Dr. Leonard has published extensively in the fields of toxicology, cell biology and immunology. In addition to section editor at Heliyon, he is also associate editor for the journal Toxicology in Vitro.

Physics

Meet the full editorial team for ***Heliyon Physics***.

Prof. Gerald Cleaver

Gerald B. Cleaver earned his Ph.D. in early universe cosmology and string theory at Caltech. He is a professor and graduate program director of the department of physics at Baylor University in Waco, Texas. He also heads the Early Universe Cosmology and String Theory (EUCOS) division of Baylor's Center for Astrophysics, Space Physics and Engineering Research (CASPER).

With CASPER colleagues, Prof. Cleaver (i) explores quantum gravity effects in the early universe and the signatures of specific quantum gravity proposals, especially with regard to the cosmic microwave background (CMB), (ii) studies relativistic thermodynamics and physics & cosmology applications to cryptography, (iii) analyzes spacetime curvatures (and their possible divergences) for theorized spacetime wormholes, and (iv) investigates advanced spacecraft propulsion systems. Prof. Cleaver was a member of a NASA blue-ribbon review committee for advanced propulsion system proposals. He has written over 100 journal articles and conference proceedings, is co-author of an elementary particle physics textbook, author of six book chapters, on the editorial board of four science journals, and referee for nine physics journals.

Psychology

Meet the full editorial team for ***Heliyon Psychology***.

Dr. Pavica Sheldon

Prof. Pavica Sheldon received her PhD in communication studies from Louisiana State University, and currently serves as chair and associate professor in the Department of Communication Arts at University of Alabama in Huntsville. Dr. Sheldon is an author of three books and over 40 journal articles, studying uses and gratifications of social media, and also how people communicate forgiveness in interpersonal relationships.

Quantitative biology, biotechnology and bioengineering

Meet the full editorial team for ***Heliyon quantitative biology, biotechnology and bioengineering***.

Dr. Andrea de Martino

Andrea De Martino received his PhD in theoretical physics from SISSA (Trieste, Italy). He worked at the Hahn-Meitner-Institut (Berlin, Germany), the Italian Institute for the Physics of Matter (Rome, Italy) and Sapienza University (Rome) before joining the National Research Council and, more recently, the Italian Institute for Genomic Medicine in Turin, where he is part of the Statistical Inference & Computational Biology Unit.

Dr. De Martino is generally interested in the physics of living systems across multiple scales, from single cells to ecosystems. He works in broadly defined systems biology (computational & mathematical biology, genome-scale models, bioinformatics, etc.). Dr. De Martino's favorite questions revolve around the functional roles of cell-to-cell heterogeneities, the interplay between physiology and gene expression in proliferating vs quiescent cells, the processing of information by biological networks, and the emergence of multi-cellular and population-level behavior.

Social science

Meet the full editorial team for ***Heliyon Social science***.

Prof. P. Vigneswara Ilavarasan

P. Vigneswara Ilavarasan (PhD - IIT Kanpur) is a professor of information systems at the Dept. of Management Studies, Indian Institute of Technology Delhi. He researches and teaches about the interaction of information and communication technologies (ICTs), society, and business.

Dr. Ilavarasan has been a visiting research fellow at United Nations University - School of Computing and Society (Macau) and School of Management, Curtin University (Perth). He is a recipient of the Outstanding Young Faculty Fellowship Award at IIT Delhi and Prof. M.N. Srinivas Memorial Prize of the Indian Sociological Society. He is also a senior research fellow at LIRNEasia, a leading regional ICT policy and regulation think tank. He has received large research grants from Dept of Science & Technology (Govt of India), ICSSR (India), IDRC (Canada), Oxford Analytica (UK), IPTS (European Commission), CIPPEC (Argentina) and IdeaCorp (Philippines). His research has appeared in various leading international journals and at numerous global conferences.

Dr. Tomayess Issa

Dr. Tomayess Issa is a Senior Lecturer at the Faculty of Business and Law - Curtin University/Australia. Tomayess completed her doctoral research in Web development and Human Factors. As an academic, she is also interested in establishing teaching methods and styles to enhance the students' learning experiences and resolve problems that

students face. Tomayess is a Conference and Program Co-Chair of the IADIS International Conference on Internet Technologies and Society and IADIS International Conference on International Higher Education. Furthermore, she initiated the IADIS conference for Sustainability, Green IT and Education. Currently, she conducts research locally and globally in Human-Computer Interaction, Usability, Social Networking, Sustainability, Sustainable Design, Green IT, Cloud Computing and Teaching and Learning. Tomayess published her work in several peer-reviewed journals, books, book chapters, papers and research reports and participated in local and global conferences. Tomayess Issa was a coordinator in the International research network (IRNet-EU (Jan2014 – Dec 2017)) to study and develop new tools and methods for advanced pedagogical science in the field of ICT instruments, e-learning and intercultural competences. Tomayess Issa is a senior research member of ISRLAb (Information Society Research Lab) from International Association for Development of the Information Society. Finally, Tomayess supervised PhD, Master of Phil and Master Dissertations; and she received Curtin Guild Awards for her teaching and supervision. In 2017, she received the overall winner Student Guild Outstanding Achievement in Teaching Excellence 2017 Award for university-wide. Tomayess received 2021 Green Gown Awards Australasia -Next Generation Learning and Skills - Highly Commended to the Green Information Technology and Sustainability unit.

Assoc. Prof. Dimitris Tsarouhas

Dimitris Tsarouhas, PhD is Visiting Associate Professor at the Department of Political Science, Virginia Tech, and Associate Professor at the Department of International Relations, Bilkent University, Turkey. He is a Non-Resident Senior Research Fellow at the Hellenic Foundation for European and Foreign Policy (ELIAMEP) and a Scientific Council Member of the Foundation for European Progressive Studies (FEPS) in Brussels.

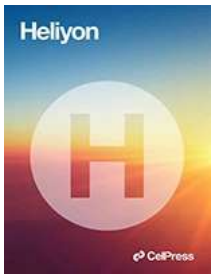
Tsarouhas is the co-editor (with Owen Parker) of Crisis in the Eurozone Periphery: The Political Economies of Greece, Spain, Portugal and Ireland (London: Palgrave 2018), author of Social Democracy in Sweden: the Threat from a Globalized World (London and New York: I.B. Tauris, 2008) and co-editor of Bridging the Real Divide: Social and Regional Policy in Turkey's EU Accession Process (METU Press 2007). His research has been published in numerous book volumes and journals such as Regulation & Governance, New Political Economy, Journal of European Integration, Public Administration, Comparative European Politics, Cambridge Review of International Affairs, Social Politics, Social Policy & Administration, Political Studies Review, Armed Forces & Society, European Journal of Industrial Relations and Southeast European and Black Sea Studies.

Women's health

Meet the full editorial team for ***Heliyon Women's health***.

Dr. Lena Serghides, PhD

Lena Serghides is a Senior Scientist at the Toronto General Hospital Research Institute, University Health Network, an Assistant Professor in the Department of Immunology and a Member of the Institute of Medical Sciences at the University of Toronto, and an Adjunct Scientist at the Women's College Research Institute, Women's College Hospital. She received a B.Sc. in. Biology from Wilfrid Laurier University and a Ph.D. in Medical Sciences from the University of Toronto. Her lab's research is motivated by the goal of optimizing maternal and infant health in the context of infections of global health importance including HIV and malaria. Her current research focus is on understanding the mechanisms that contribute to the increased risk for adverse pregnancy outcomes in women living with HIV – with a special focus on the placenta, as well as understanding the long-term effects of in utero exposure to HIV and HIV antiretrovirals.



Apr 01, 2022
Volume 8, Issue 4
Open Access

Research article

Microbial contamination of diesel-biodiesel blends in storage tank; an analysis of colony morphology
Leily Nurul Komariah, Susila Arita, Muhammad Rendana, Cindi Ramayanti, Ni Luh Suriani, Desi Erisna
e09264
Full-Text HTML | PDF

Extraction of Th(IV) metal ions with trioctylphosphine oxide dissolved in kerosene using multi-dropped liquid membrane technique
Ramazan Donat, Emrah Tavşan
e09258
Full-Text HTML | PDF

Green-synthesized, pH-stable and biocompatible carbon nanosensor for Fe^{3+}: An experimental and computational study
Savan K. Raj, Babita Choudhary, Anshul Yadav, Rajesh Patidar, Avinash Mishra, Vaibhav Kulshrestha
e09259
Full-Text HTML | PDF

Transesterification of Yellow Oleander seed oil, its utilization as biodiesel and performance evaluation
Subhrajyoti Bhattacharyya
e09250
Full-Text HTML | PDF

Determination of the influence of weather and air constituents on aortic aneurysm ruptures
Irena Kaspar-Ott, Patrick Olschewski, Stephanie Koller, Alexander Hyhlik-Duerr, Elena Streck, Hans-Henning Eckstein, Oksana Radu, Elke Hertig
e09263
Full-Text HTML | PDF

Nigella sativa L. as immunomodulator and preventive effect on renal tissue damage of lupus mice induced by pristane
Zahrah Hikmah, Anang Endaryanto, I. Dewa Gede Ugrasena, Anny Setijo Rahaju, Syaiful Arifin
e09242
Full-Text HTML | PDF

Groundwater quality evaluation for domestic and irrigation purposes for the Nwanedi Agricultural Community, Limpopo Province, South Africa
Mulaudzi Mukonazwothe, Linton Fhatuwani Munyai, Mulalo Isaih Mutoti
e09203
Full-Text HTML | PDF

PEGylated aceclofenac solid lipid microparticles homolipid-based solidified reverse micellar solutions for drug delivery
Calister E. Ugwu, Jude N. Oraeluno, Kingsley C. Eze, Caleb O. Ezenma, Anthony O. Nwankwo
e09247
Full-Text HTML | PDF

Transduodenal resection for duodenal adenomas may be an underutilized tool – A single institution experience
Shankar Logarajah, Edward E. Cho, Peter Deleeuw, Houssam Osman, D. Rohan Jeyarajah
e09187
Full-Text HTML | PDF

Investigating the anti-inflammatory and analgesic properties of leaves ethanolic extracts of *Cedrus libani* and *Pinus brutia*
Lina Karrat, Mohammad Yaser Abajy, Ream Nayal
e09254
Full-Text HTML | PDF

Does *Islamicity* matter for the stability of Islamic banks in dual banking systems?
Abderazak Bakhouche, Teheni El Ghak, Mohammad Alshiab
e09245
Full-Text HTML | PDF

Assessment of indigenous Shaka cattle structural indices reared in Shaka zone, south west Ethiopia
Worku Masho, Sandip Banerjee, Mestawet Taye, Zelalem Admasu, Mekuanent Baye
e09212

Heliyon 8 (2022) e09242

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Nigella sativa L. as immunomodulator and preventive effect on renal tissue damage of lupus mice induced by pristane

Zahrah Hikmah [a,b,c,*], Anang Endaryanto [b,c], I. Dewa Gede Ugrasena [b,c], Anny Setijo Rahaju [c,d,e], Syaiful Arifin [f]

[a] Medical Doctoral Program Student, Faculty of Medicine, Universitas Airlangga, 60132, Surabaya, Indonesia
[b] Division of Allergy and Immunology, Departments of Pediatric of Medicine Universitas Airlangga, Surabaya, Indonesia
[c] Dr. Soetomo Academic Teaching Hospital, 60286, Surabaya, Indonesia
[d] Universitas Airlangga Academic Hospital, Surabaya, Indonesia
[e] Department of Anatomical Pathology, Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia
[f] Postgraduate School of Biomedicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

ARTICLE INFO

Keywords:
Nigella sativa L.
Immunomodulator
Lupus
Renal

ABSTRACT

Introduction: *Nigella sativa* L. is an herbal plant with Thimoquinone as the main therapeutic properties. This plants has been shown to cure for various diseases and affected the immune system by modulating cytokines and T regulatory cell (Treg) sot that able to prevent renal injury in several diseases, but studies on Systemic Lupus Erythematous are still rare.
Objective: This study aimed to investigate immunomodulation and preventive effects of *Nigella sativa* L. on renal tissue damage in Pristane induced Lupus (PIL)-mice model.
Methods: This true experimental study included 48 female Balb/C mice, 38 mice were injected pristane intraperitoneally and waited 16 weeks to become lupus model. Only 30 mice met the Systemic Lupus International Collaborating Clinics criteria. Ten healthy mice were used as control, 30 PIL mice model divided into 3 groups (placebo, steroid, *Nigella sativa* L.). At the end of 28 days of treatment, the mice were sacrificed to take a blood sample and kidney organ to evaluate the injury histopathologically.
Results: The results showed that the cytokine expression Interleukin (IL) (IL-17, IL-6, IL-23) in the *Nigella sativa* L. group was the lowest. The highest absolute number of Tregs was the steroid group followed *Nigella sativa* L. group. Renal injury assessed histopathologically showed the *Nigella sativa* L. group was the lowest and almost close to normal.
Conclusion: This study indicate that *Nigella sativa* L. has an immunomodulatory effect and can prevent kidney injury PIL-treated mice. We suggest that *Nigella sativa* L. may need to be considered for further research on its use as a complementary supplement in lupus patients.

1. Introduction

Systemic Lupus Erythematous (SLE), is a chronic autoimmune disease, with the main problem is the dysregulation of the immune system and its response to self-antigens, causing damage to various organs and tissues (La Paglia et al., 2017; Kaul et al., 2016). In some studies, the prevalence of renal injury in SLE is 41–55% (Hiraki et al., 2008; Osio--Salido and Manapat-Reyes, 2010; Hamijoyo et al., 2019), is mainly associated with the disorder of the immune system, deposition of immune complexes in the tissues resulting in inflammation and secretion of pro-inflammatory cytokines (Yap and Lai, 2010; Cunha and Gilek-Seibert, 2016). Consequently, alternative treatment is needed to protect the renal, such as an immunomodulator. Immunomodulation is interpreted as a temporary alert in certain parts of the immune system which can change caused by the agents that activate or suppress its function, and acts to regulates the immune system (Wen et al., 2012).

Glucocorticoid and immunosuppressant are still the main drugs that signify applied in SLE with broadside effects that are not specific, so that long-term use will cause severe problems for SLE patients and even lead to death (Kudo, 2015; Giraldo et al., 2012; Amissah-Arthur and Gordon, 2010). Lupus drug side effects vary widely depending on dosage and the length of treatment. For a long time using, it leads to clinical

* Corresponding author.
E-mail address: dr.zahrah.spa@gmail.com (Z. Hikmah).

https://doi.org/10.1016/j.heliyon.2022.e09242
Received 9 August 2021; Received in revised form 27 November 2021; Accepted 31 March 2022

complications such as secondary infection, cataracts, musculoskeletal diseases including osteoporosis, vascular necrosis, and myopathy, and also cardiovascular complications such as myocardial infarction and cerebrovascular disease (Oon et al., 2018; Sinha and Bagga, 2008; Kasturi and Sammaritano, 2016). It is necessary to find an alternative source with effective, safe, cheaper immunomodulator agents for SLE patients.

Nigella sativa L., also known in Indonesian as Habatussauda or Jinten Hitam (Black Cumin), has been utilized for resolving numerous diseases since hundreds of years ago and was generally used in traditional medicine (Kabir et al., 2020). *Nigella sativa* L., seeds contain fixed oil, proteins, alkaloids, saponins, and essential oil. There are variant of compounds present in *Nigella sativa* L., including thymoquinone (TQ), thymohydroquinone, dithymoquinone, p-cymene, α-thujene, γ-terpinene, carvacrol, α-pinene, β-pinene, 4-terpineol, and sesquiterpene longifolene, carvone, limonene, and citronellol. TQ is one of the active compounds in *Nigella sativa* L. and it has been widely investigated in various diseases. Previous studies of *Nigella sativa* L. showed antimicrobial, antibacterial, antifungal, antiparasitic, anticancer, anti-Inflammatory, and immunomodulatory activities (Kabir et al., 2020; Islam et al., 2017). The biological effects of *Nigella sativa* L. are attributed to the various experimental studies on animal models have proven that it acts as the immunomodulator in autoimmune diseases by reducing cluster of differentiation (CD)8+ and increasing the percentage of CD4+ CD25+ T cells in rheumatoid arthritis (RA) patients (Kheirouri et al., 2016). It also proved to increase the percentage of Treg and decreased T helper (Th)17 in asthma mice models (Barlianto et al., 2012). *Nigella sativa* L. powder can modulate the immune response by lowering IL-23 in people with Hashimoto's thyroiditis (Tajmiri et al., 2016) and production of autoantibodies in several other autoimmune diseases (Hmza et al., 2013; Farhangi et al., 2016). Moreover, it can also be used to protect the kidney from various diseases. However, the immunomodulatory and preventive effect of *Nigella sativa* L. in renal tissue of SLE patient has not been studied in a systematic context. Therefore, this study was done to evaluate the immunomodulator and renal tissue preventive effect of *Nigella sativa* L. extract in the lupus mice model.

2. Material and methods

2.1. Animals

BALB/c female mice (age 6–8 weeks, 20–30 g) have been supplied from Universitas Islam Negeri Malang, Indonesia. Animals were adapted for one week before starting the experiments under appropriate temperature, humidity, and light conditions. They were fed a common diet and very free access to libitum ad air. All mice were maintained at the Pharmacy Laboratory, Faculty of Medicine, Universitas Brawijaya, Indonesia.

2.2. Materials

Nigella sativa L. was obtained from Materia Medica Batu, Malang, Indonesia, and extracted at the Pharmacy Laboratory, Universitas Airlangga, Indonesia. *Nigella sativa* L. seeds were ground and then extracted with ethanol solvent using the soxhletation method. The resulting mixture was vortexed for 1 min and sonicated for 20 min. In addition, incubated with ethanol solution for 24 h in a constant rotamix and Soxhlet machine, then vortexed again for 1 min and centrifuged for 25 min at 1400 rpm. The content of TQ in the extracted *Nigella sativa* L. was examined for levels using the High-Performance Liquid Chromatography (HPLC) method. The centrifuged supernatant of 20 L was injected into the HPLC machine in the water-ethanol mobile phase (25 + 75, v/v) with a flow rate of 1 mL/min. Quantification was achieved by UV-Vis Spectroscopy detection at 254 nm. A 0.2%. Sodium Carboxymethyl Cellulose (Na CMC) solution was prepared by weighing 40 mg of Na CMC. Prepare about 20 ml of hot water in a mortar. Sprinkle 40 mg of Na CMC into 20 ml of hot water in a mortar and grind it well. This liquid is used to disperse steroids according to the dose used then given with a forced feeding as much as 0.5 ml. Pristane was given 0.5cc intraperitoneally for each mouse and was obtained from Sigma-Aldrich, Singapore for this study.

2.3. Experimental design

The study design was a randomized post-test-only control group design. The PIL-treated mice are developed within 16 weeks after a 0.5 cc single intraperitoneal pristane injection and fulfill Systemic Lupus International Collaborating Clinics (SLICC) criteria (alopecia, arthritis characterized by swelling of 2 or more joints, and increased anti-dsDNA autoantibodies). Pristane can induce systemic lupus with a variety of symptoms such as organ involvement and autoantibodies in a variety of mouse strains. Pristane intraperitoneal injection will stimulate the formation of autoantibodies associated with lupus in the face of multiple nuclear antigens (Yan et al., 2020; Freitas et al., 2017; Li et al., 2017). BALB/c female mice were divided into four groups which are categorized into healthy group and 3 treatment groups. The treatment groups are Placebo group (PIL+ Na CMC 0.2% for 28 days-intragastrical), Steroid group (PIL + Prednisone 0.346 mg-0,369 mg (converted from human dose 1 mg/kg + Na CMC 0.2% for 28 days-intragastrical) and *Nigella sativa* L. group (PIL+ extract *Nigella sativa* L. 4.8 g/kg/day + Na CMC 0.2% for 28 days-intragastrical). On the first day of the 21st-week treatment, the mice were sacrificed to take the blood sample and to remove the renal organ for blood and histopathological evaluation.

2.4. Blood evaluation

The autoantibody concentrations against double stranded deoxyribonucleic acid (dsDNA) were measured by enzyme-linked immunosorbent assay (ELISA) microplate reader. Flat-bottomed 96-well plates coated with recombinant human dsDNA, sample buffer, wash buffer, tetramethylbenzidine substrate, and stop solution (1M HCl) were provided by Aesku Diagnostics (Wendelsheim, Germany). An antibody detection (horseradish peroxidase-conjugated goat anti-mouse IgG) was purchased from Chemi-Con. Diluted probes (1:500 and 1:5000; standard probes were continuously diluted in sample buffer to set a standard curve) were incubated for 1 h at room temperature and, after 3 washing steps, were subsequently incubated with detection antibody (peroxidase-labeled goat anti-mouse Immunoglobulin (Ig)G, dilution 1:1000 in diluent buffer, Chemicon) for 15 min at room temperature. After 3 additional washing steps, 100 μl of tetramethylbenzidine substrate was added. After 15 min, the reaction was stopped by adding 100 μl of stop solution (1M HCl). Finally, optical density was determined with an ELISA reader (Rainbow reader; SLT Labinstruments, Groding, Austria) at the wavelength of 450 nm. Analyses were performed in duplicate treatment. Anti-dsDNA titers are given as units per milliliter. IL-6 expression was measured based on the count relative percentage of IL-6 expressed by macrophage using IL-6 PE/Cy5.5-conjugated anti-mouse IL-6 (trademark Clone NBPI, Novus biologicals, LLC). CD11b is the marker of macrophage surface cells, were measured using CD11b FITC anti-mouse/human CD11b (clone: M1/70, BioLegend). The measurement of IL-6 was conducted using flow cytometry. IL-17 expression was measured based on the count relative percentage of IL-17 expressed by Th-17 using IL-17 marker PerCP/Cy5.5 anti-mouse IL-17A (Trademark Clone TC11-18H10.1, BioLegend). CD4 is the marker of T helper (Th) cells surface, were measured using FITC anti-mouse CD4 (Trademark Clone H129.19, BioLegend). The measurement of IL-17 was conducted using flow cytometry. IL-23 expression was measured based on the count relative percentage of IL-23 expressed by macrophage using PE-conjugated rat antimouse IL-23 (Trademark Alexa Fluor 488, eBioscience). The measurement of IL-23 was conducted using flow cytometry. CD11b is the marker of macrophage surface cells, were measured using CD11b Monoclonal Antibody (trademark Thermo Fisher Scientific, BioLegend). The Treg cells were count based on the percentage of absolute count of

Treg cells: CD4 + CD25 + FoxP3 + IL-10 multiply by total lymphocyte cells. CD4 were measured using FITC anti-mouse CD4 (clone H129.19, BioLegend), CD25 were measured using PE anti-mouse CD25 (clone: 3C7, BioLegend), FoxP3 were measured using Alexa FluorR 647 anti-mouse/rat/human FOXP3 (Trademark Clone: 150D, BioLegend), and IL-10 were measured using PE/Cy7 anti-mouse IL-10 (trademark Clone: JES5-16E3, BioLegend).

2.5. Histopathology findings

Renal of mice were fixed by immersing them in 10% Neutral buffered formalin (NBF) solution for 24 h and cutting the tissue with a maximum size of 1 × 1 cm. Tissue was taken from 10% NBF solution and placed to the 70%, 80%, 90% alcohol solution for 1 day, respectively. Then, it is purified and replaced with xylol chemicals that possibly mixed with dehydrants and paraffins. The tissue was immersed in the xylol solution 2 times for 30 min (xylol I 30 min, xylol II 30 min). Then do immersion (infiltration/impregnation/embedding). The tissue was put in liquid paraffin at 56–60 °C for 3 × 1 h in an incubator (paraffin I 1 h, paraffin II 1 h, paraffin III 1 h). After Blocking/Casting, the tissue was inserted into the printer and then put into the cube and paraffin chamber. The paraffin blocks were stored overnight and sliced using a microtome with a thickness of 5–10 m and then placed in a water bath at 50 °C. After the paraffin tape was well developed, attach the paraffin tape to an object-glass coated with albumin + glycerin, dry and Hematoxylin and Eosin (HE) and Periodic acid–Schiff (PAS) staining processes. The preparations were affixed with a cover glass which had been added with a single drop of Canadian balsam. The preparations were viewed using a binocular microscope Then, light microscopy observations make under a binocular microscope—the finding record at the initial magnification of x400. The degree of renal damage was based on histopathology, while the classification was based on the International Society of Nephrology and the Renal Pathology Society (ISN/RPS) classification of Lupus Nephritis (LN) (Pinheiro et al., 2019; Sada and Makino, 2009). Organ fragments are printed by a pathologist expert using the LN activity index (AI) method by the National Institutes of Health (NIH). NIH-AI is a semi-quantitative grading system of pathologic features on renal biopsies that allows for monitoring response for treatment and showing disease progression. LN disease activity can be assessed on a renal biopsy using the modified NIH activity and chronicity indices. Indicators of disease activity involve endocapillary hypercellularity, neutrophils or karyorrhexis within glomerular capillary loops, fibrinoid necrosis, hyaline deposits, cellular or fibro cellular crescents, and interstitial inflammation. Crescents and fibrinoid necrosis are weighted twice as they have a worse impact on prognosis. The scoring is referred to the percentage of glomeruli with each feature in the biopsy on a scale of 0–3, with a score of 0 = not present, 1 = <25% glomeruli, 2 = 25–50% glomeruli, and 3 indicating >50% glomeruli. NIH-AI was used to measure the progression of LN (Bajema et al., 2018; Fava and Petri, 2019).

2.6. Assessment of CD34 cells by flow cytometry

All spleen is crushed and homogenized in a mortar using the sterile pestle as well as a fine mesh metal sieve inside a Petri dish added with phosphate buffer salt (PBS). Then, the suspension of the existing cells is inserted into the Falcon tube and centrifuged (2500 rpm, for 5 min at 10 °C) with a fried centrifuge (Hermle Z326K). Then eliminate the supernatant. Pellets containing spleen are inserted into microtubes with PBS and dicryopreserved using fetal bovine serum (FBS) and dimethyl sulfoxide (DMSO) with a maximum duration of 14 days until further evaluation using flow cytometry. Showing the flow cytometry experiments, so splenocytes unfroze. Resuspend using RPMI medium 1640 at room temperature, then rinsed and centrifuged (1500 rpm for 10 min at 4 °C) twice, then resuspended using FBS and PBS. Stained samples are stored for 1 h in darkrooms at 4 °C–8 °C with CD34 anti-mouse monoclonal Abs (BD Biosciences). Cells were permeabilized using Biolegend as permeabilization buffer with a ratio of 1:10 for dilution on stains for intracellular Foxp3. Shortly after incubation with monoclonal abs, then the sample is centrifuged and washed using PBS and then repaired using 4% paraformaldehyde. Then conducted flow cytometry analysis using flow cytometer BD FACS Calibur.

2.7. Statistical analysis

Statistical analysis was conducted using SPSS version 25. Normality test and homogeneity test was done to determine the data distribution using Shapiro-Wilk test, and continue with: The one-way ANOVA, for a normal variable with distribution and homogenous, post hoc using LSD multiple comparison Kruskal-Wallis test, for normal distribution but not homogenous, post hoc analysis using the Mann-Whitney U test.

2.8. Research ethics

This study was performed under ethical standards for animal experimentation, and the Ethical Committee approved it, Faculty of Veterinary Medicine, Universitas Airlangga, Indonesia (Ethical Clearance No. 2.KE.165.08.2019).

3. Results

Forty-eight mice were recruited and 38 mice were injected with pristine-intraperitoneal. Only 30 mice still alive and have been successfully fulfilled SLICC criteria lupus. Ten mice were used as healthy group. The profile of animal subjects was summarized as follows.

3.1. Serum levels of anti-dsDNA antibodies

The mean results of measuring serum levels of anti-dsDNA antibodies in Healthy, Placebo, Steroid, and *Nigella sativa* L. groups are presented in Table 2 and Figure 1. The mean serum levels of anti-dsDNA antibodies were higher in the Placebo group compare to the Healthy, Steroid, and *Nigella sativa* L. groups. From the results o, a p-value of <0.001 showed that there were at least two groups that were significantly different. From the results of the test between groups, the mean levels were significantly higher in the Placebo group (57.88 ± 0.84) compared to the Healthy group (45.32 ± 2.56; $p < 0.001$), Steroids (52.86 ± 1.80; $p < 0.001$) and *Nigella sativa* L. group (49.01 ± 1.17; $p < 0.001$). Anti-dsDNA antibody levels in the *Nigella sativa* L. group were significantly lower compared to the Steroid group ($p < 0.001$).

3.2. IL-17 expression of lupus mice models

The IL-17 expression represents as the percentage of CD-4^+ IL-17^+ as summarized at Figure 1 and Table 2. The percentage of IL-17 expression is significantly higher in Placebo group (2.51 ± 0.72) compared to Healthy (0.89 ± 0.52, $p < 0.001$), Steroid (1.39 ± 0.27, $p < 0.001$) and *Nigella sativa* L. group (0.97 ± 0.31; $p < 0.001$). The percentage of IL-17 expression is lower at *Nigella sativa* L. group than Steroid group (0.97 ± 0.31 vs 1.39 ± 0.27 vs., $p < 0.05$).

3.3. The IL-6 expression of lupus mice models

The result of the IL-6 expression is presented as the average percentage of CD-$11b^+$ IL-6^+, as summarized in Table 2 and Figure 1. The placebo group has a higher IL-6 level compared to the Healthy, Steroid, and *Nigella sativa* L. group ($p < 0.001$). Expression of IL-6 was higher at Placebo group (2.39 ± 0.50) compared to Healthy (0.21 ± 0.09) Steroids (0.49 ± 0.07; $p < 0.001$) and *Nigella sativa* L. group (0.29 ± 0.06, $p < 0.001$). IL-6 expression on the *Nigella sativa* L. group was notably lower than the Steroid group (0.29 ± 0.06 vs 0.49 ± 0.07, $p < 0.001$).

3.4. The IL-23 expression of lupus mice models

The average expressions of IL-23 between the three groups were summarized in Table 2 and Figure 1. IL-23 at placebo group was higher compared to Healthy, Steroid, and *Nigella sativa* L. groups. The result of the IL-23 expression is presented as the average percentage of CD-11 b^{+} IL-23^{+}. In Figure 2. The LSD multiple comparisons showed that the Placebo group has IL-23 level (5.17 ± 0.39) higher significantly than Steroid (3.20 ± 0.59%, $p < 0.05$) and *Nigella sativa* L. group (1.60 ± 0.57%, $p < 0.001$), and the IL-23 expression of *Nigella sativa* L. group is significantly lower than Steroid group (1.60 ± 0.57 vs 3.20 ± 0.5, $p < 0.001$).

3.5. Treg expression of lupus mice models

The mean absolute Treg cell count was higher in the Steroid group compare to *Nigella sativa* L. and Placebo groups. The results of the normality test of the data using the Shapiro-Wilk test showed that the data had a normal distribution ($p > 0.05$), while the results of the Levene homogeneity test showed that the data were not homogeneous ($p < 0.05$) so that the Brown-Forsythe substitute test was used for assessing at the differences between the two groups. From the results of the Brown-Forsythe test, a p-value of <0.001 ($p < 0.05$) was obtained, which indicated that there were at least two groups that were significantly different. Test between groups is also needed to determine the value of

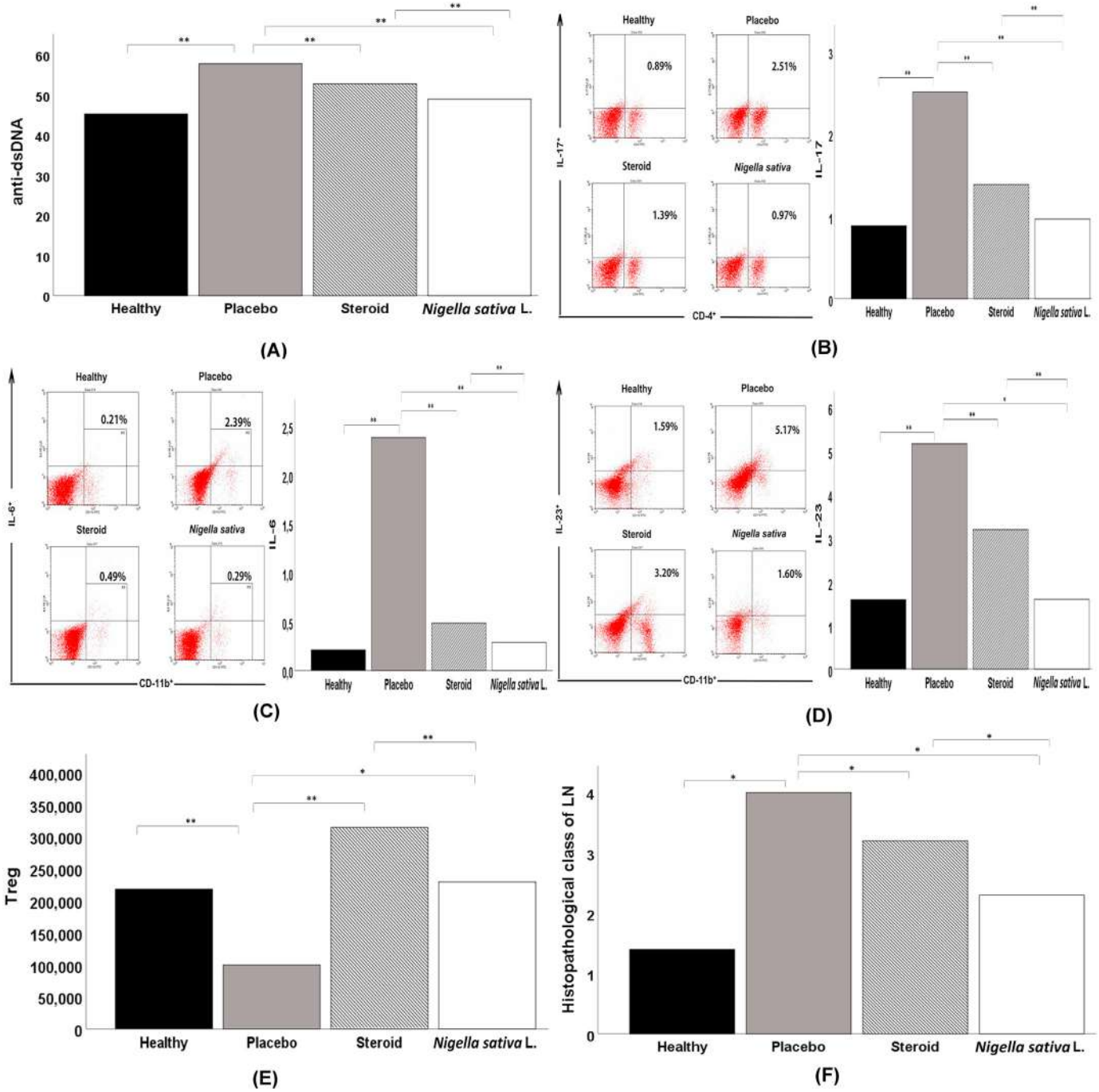


Figure 1. A) Anti-dsDNA analysis of all experimental groups, B) IL-17 analysis of all experimental groups, C) IL-6 analysis of all experimental groups, D) IL-23 analysis of all experimental groups, E) Treg analysis of all experimental groups, F) Histopathological Class of LN analysis of all experimental groups. Significant effect is indicated by asterisk (*, $p < 0.05$; **, $p < 0.001$).

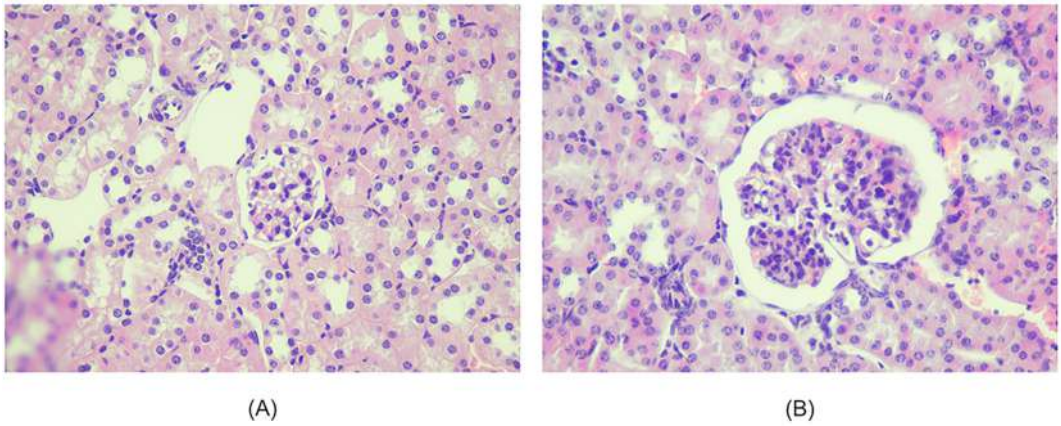


Figure 2. Histopathological view of renal sections in Healthy and treatment groups with HE (Hematoxylin and Eosin) staining, 400 HPF (A) The healthy group showed minimal mesangial matrix enhancement (B) The Placebo group showed hypercellular mesangial matrix, mesangial expansion, endocapillary hypercellularity dan infiltration of neutrophils.

differences between groups. From the results of the Games-Howell multiple comparisons test, the mean was significantly higher in the Steroid group (314,182.38 ± 119,942.73) compared to the Placebo group (99,528.76 ± 56,395.11; $p < 0.001$) as well as with the *Nigella sativa* L. group (229,322.63 ± 54,432.00, $p < 0.001$). The mean absolute number of Treg cells in the *Nigella sativa* L. group was strongly higher when compared to the Placebo group as shown in Table 2.

3.6. Effect of Nigella sativa L. on histopathological renal tissue

Histopathological changes of renal in all groups are shown in Figures 1, 2, 3, and 4. Microscopic examination of the Healthy group revealed normal renal glomeruli and minimal mesangial matrix enhancement (Figures 1 and 2). However, renal tissue damage is seen in the case of intraperitoneal injection of pristane. Diffuse hypercellular endocapillary, mesangial hypercellular, thickened capillaries and closed vascular endothelium were observed in the Placebo group (Figures 1 and 2). Mild histopathological lesions were observed in the Steroid and *Nigella sativa* L. groups (Figures 3 and 4). Observation of histological preparations showed that there was protective of renal structural damage in the Steroid and *Nigella sativa* L. groups. To assess the magnitude of the change in pathological scores, performed to assess the renal based on the ISN/RPS classification of LN by an anatomical pathologist (shown in Table 1). The Placebo groups showed a higher grade of LN (IV [IV–IV]) compared to the Healthy group (I [I–I], $p < 0.05$). The Steroid and *Nigella sativa* L. groups showed a lower grade of LN (III [II–IV] and II [II–III], $p < 0.05$) compared to the Placebo group. The severity of tissue damage in the renal of *Nigella sativa* L. group was considerably lower when compared to the Placebo and Steroid ($p < 0.05$) groups.

3.7. Effect of Nigella sativa L. on Activity Indices

The effect of Placebo (carboxymethyl cellulose sodium 0.2%), Steroid (Prednisone), and *Nigella sativa* L. on renal Activity Index (AI) are shown in Table 2. Compared with the Healthy group, Placebo presented with significantly higher AI (4.5 [1–5] vs. 2 [0–3], $p < 0.05$). The Steroid group has lower AI when compared to the Placebo group (3 [2–4] vs. 4.5 [1–5], $p < 0.05$). *Nigella sativa* L. group significantly has lower AI when compared to Placebo or Steroid groups (2 [1–3] vs. 4.5 [1–5] or 3 [2–4], respectively, $p < 0.05$).

3.8. Effect of Nigella sativa L. on CD34+ cells

Means (±SD) of the data obtained in all groups are given in Table 3. The Placebo group showed significantly lower CD34+ cells compared to the Healthy group (46.0 ± 31.69 vs. 79.0 ± 9.94, $p < 0.05$). The steroid group has higher CD34+ cells significantly when compared to the Placebo group (57.0 ± 18.88 vs. 46.0 ± 31.69, $p < 0.05$). *Nigella sativa* L. group significantly has higher CD34+ cells when compared to Placebo and Steroid groups (76.5 ± 10.55 vs. 46.0 ± 31.69, and 57.0 ± 18.88, respectively, $p < 0.05$).

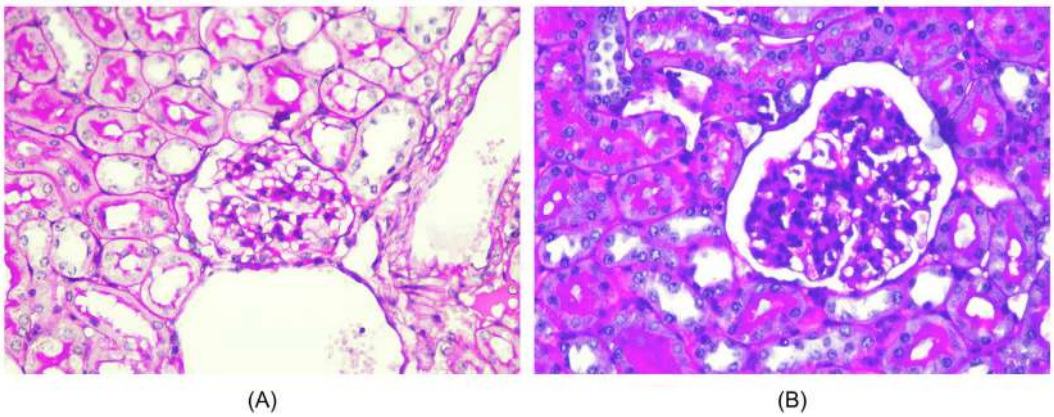


Figure 3. Histopathological slide of renal sections in Healthy and Placebo groups with PAS (Periodic acid–Schiff) staining, 400HPF. (A) The healthy group showed minimal mesangial matrix enhancement. (B) The placebo group showed hypercellular mesangial matrix, mesangial expansion, endocapillary hypercellularity dan infiltration of neutrophils.

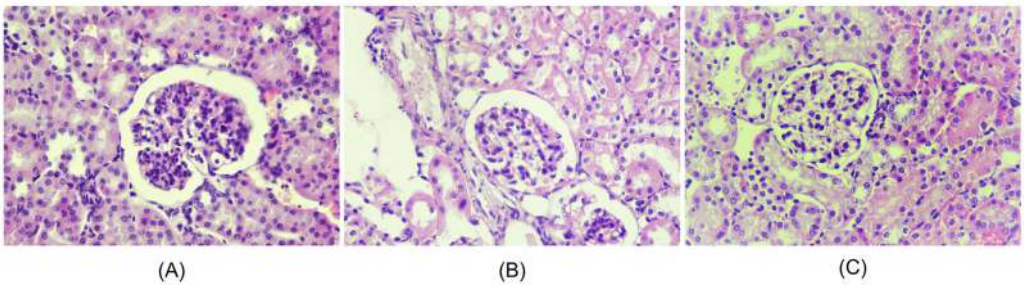


Figure 4. Histopathological slide of renal sections in Placebo, Steroid, and *N.sativa* groups (HE, 400 HPF). (A) The placebo group showed diffuse hypercellular mesangial, mesangial expansion, endocapillary hypercellularity dan infiltration of neutrophils. (B) The steroid group showed hypercellular mesangial matrix and mesangial expansion, without other abnormalities. (C) *Nigella sativa* L. group showed hypercellular mesangial matrix and minimally mesangial expansion appearance.

4. Discussion

Nigella sativa L. is well known as a cure for various diseases and had been proved to affects the immune system by modulating cytokines and Tregs (Prastiwi et al., 2015; Suprijono and Paramita, 2021; Shaterzadeh-Yazdi et al., 2018a, 2018b; Arjumand et al., 2019). Cytokines such as IL-6, IL-23, IL-17, and Tregs that take a part in the SLE pathogenesis, *Nigella sativa* L. have been proven to modulate these cytokines and eliminate organ damage (including renal) in various diseases but the information about the effect on SLE is limited (Tackey et al., 2004; Dolff et al., 2011; Crispín et al., 2010; Rönnblom and Elkon, 2010). The present study is the first investigation that evaluates the effect of *Nigella sativa* L. as an immunomodulator and renal tissue preventive in SLE.

The IL-6 expression in *Nigella sativa* L. group is significantly lowest than other groups, which is similar to another animal study (Umar et al., 2012). Other in vivo study showed TQ in *Nigella sativa* L. able to inhibit TNF-α-induced IL-6 production (Amissah-Arthur and Gordon, 2010) and reduce the expression of IL-4, IL-5, IL-6, and TGF-b1 mRNA in the rat model of allergic airway inflammation (Shahzad et al., 2009). *Nigella sativa* L. group showed the lowest expression of IL-17 compared to other groups, which are consistent with study conducted in non-lupus diseases (Agustiarini et al., 2019). In contrast to the results of research on asthma patients conducted by Salem et al., which found that giving *Nigella sativa* L. could not significantly reduce IL-17 levels (Kheirouri et al., 2016; Salem et al., 2017). Others stated that *Nigella sativa* L. has no effect on Th17 which is the largest producer of IL 17A (Li et al., 2015).

This study showed that *Nigella sativa* L. group had the lowest expression of IL-23 compared to other treatment groups, which is supported by Tajmiri et al. (2016) study in Hashimoto's thyroiditis patients for 8 weeks. *Nigella sativa* L. decreased the expression of IL-23 and transformed growth factor-β (TGF-β) (Tajmiri et al., 2016). In this study, the absolute number of Treg in *Nigella sativa* L. group was higher than placebo. This study is in line with animal research on asthma and etherical Serovars Typhimurium (Barlianto et al., 2012; Ahmed et al., 2018). In contrast, Susanti et al. (2013) found no significant change in asthmatic rats treated with *Nigella sativa* L. (Susanti et al., 2013).

It is proposed that the reduction of the cytokine after the administration of TQ is due to its role to detain interleukin-1 receptor-associated kinase 1 (IRAK1) activation. The IRAK-1 receptor, a serine/threonine receptor, acts to regulate the Toll-Like Receptor (TLR) signal and transmits it to transcription factors for the synthesis of the pro-inflammation cytokines, Nuclear factor-kappa B (NF-k), and activator protein-1 (AP-1) pathways in macrophage, Dendritic cell (DC), and T lymphocyte cells. It also provokes the differentiation of T lymphocyte cells to the pro-inflammation immune response (M1 polarization), such as Th1 and Th17 by suppressing Treg activation. So inhibiting IRAK-1 activation via IRAK-1 receptor is the potential pathway for effective intervention in inflammation disease (Susanti et al., 2013; Maitra et al., 2009). TQ, as one of the bioactive compounds of *Nigella sativa* L., is capable to suppress or inhibit the activation of IRAK-1, so the DC activation is blocked and suppressing T cell lymphoid to proliferate to Th17 and down-regulate IL-17 expression. On the other hand, the suppression of IRAK-1 stimulates Treg expression by upregulating its synthesis (Hossen et al., 2017).

In the study of pediatric SLE patients showed that renal damage is one of the most common manifestations (Hiraki et al., 2008). The degree of renal damage was based on the ISN/RPS classification of LN. *Nigella sativa* L. groups showed a significantly lowest grade of renal damage compared to steroid and placebo groups. It shows that *Nigella sativa* L. can prevent renal damage better than steroid treatment. These findings agree with the findings of other investigators who observed supplementation of *Nigella sativa* L. on renal injury in Pristane induce arthritis in Rats (Faisal et al., 2015). We evaluate the renal score of NIH- Activity Indices (AI) to measure the progression of LN (Bajema, Wilhelmus, Alpers, Bruijn, Colvin, Cook, D'Agati, Ferrario, Haas and Jennette, 2018; Fava and Petri, 2019). *Nigella sativa* L. group showed significantly lower AI than the Placebo group. These results suggest that the administration of *Nigella sativa* L. may reduce the renal inflammation caused by autoimmune mechanisms. TQ reduced oxidative stress markers such as MDA and increased antioxidant content, including malondialdehyde (MDA); superoxide dismutase (SOD); glutathione (GSH); catalase (CAT); Glutathione-S-Transferase (GST), which have a critical role in renal damage (Shaterzadeh-Yazdi et al., 2018a, 2018b).

The present study also assessed the potential effect of extract *Nigella sativa* L. by studying its effect on renal tissue damage, which was measured in terms of CD34+. Local CD34+ capillaries decrease in mouse models of renal disease associated with the severity of glomerular and tubulointerstitial lesions. *Nigella sativa* L. group shows significantly higher in CD34+ compared to Placebo group. This result showed that *Nigella sativa* L. can prevent the number of CD34+ glomerular capillaries decreased caused by the autoimmune process. *Nigella sativa* L. group is significantly increased CD34+ cells and resulted in lower AI than the Steroid and Placebo group. Several studies have shown an association between autologous transplantation of CD34-positive cells resulting in remission and reduced severity of symptoms in LN (Alchi et al., 2013; Su et al., 2013). Although this is the first study to evaluate the immunomodulatory and preventive effect on renal tissue damage of *Nigella sativa* L. in lupus, the absence of prior examination before treatment can be considered as a weakness of this study.

Table 1. The profile of subjects between mice lupus model and normal mice.

Subject's profile	Lupus model (N = 30)	Normal mice (N = 10)
Body weight (g) (post pristane)	28.11	38.16
Anti-dsDNA	55.15 ± 1.26	45.32 ± 2.56
Alopecia	30	0
Arthritis	30	0

The expression of anti-dsDNA IL-6, IL-23, IL-17, and Tregs on the lupus mice model is presented as the average value + standard deviation. All data were distributed normally ($p > 0.05$) and but not homogenous ($p < 0.05$).

Table 2. The result of dsDNA, IL-17, IL-6, IL-23, and Treg expression on Healthy, Placebo, Steroid, and *Nigella sativa* L. group.

Groups	n	dsDNA		p-value
		$\bar{x} \pm$ SD	Min-Max	
Healthy	10	45.32 ± 2.56^{a}	41.36–47.88	<0.001*
Placebo	10	57.88 ± 0.84^{b}	56.12–58.87	
Steroid	10	52.86 ± 1.80^{c}	50.99–55.91	
Nigella sativa L.	10	49.01 ± 1.17^{d}	48.03–50.71	
		IL-17		
		$\bar{x} \pm$ SD	**Min-Max**	
Healthy	10	$0,89 \pm 0,52^{a}$	0.19–1.52	<0.001*
Placebo	10	2.51 ± 0.72^{b}	1.73–3.73	
Steroid	10	1.39 ± 0.27^{c}	0.85–1.76	
Nigella sativa L.	10	0.97 ± 0.31^{d}	0.71–1.53	
		IL-6		
		$\bar{x} \pm$ SD	**Min-Max**	
Healthy	10	0.21 ± 0.09^{a}	0.09–0.34	<0.001*
Placebo	10	2.39 ± 0.50^{b}	2.03–3.59	
Steroid	10	0.49 ± 0.07^{c}	0.38–0.59	
Nigella sativa L.	10	0.29 ± 0.06^{d}	0.21–0.39	
		IL-23		
		$\bar{x} \pm$ SD	**Min-Max**	
Healthy	10	1.59 ± 0.51^{a}	0.73–2.33	<0.001*
Placebo	10	5.17 ± 0.39^{b}	4.68–5.87	
Steroid	10	3.20 ± 0.59^{c}	2.36–4.35	
Nigella sativa L.	10	1.60 ± 0.57^{d}	0.92–2.38	
		Treg		
		$\bar{x} \pm$ SD	**Min-Max**	
Healthy	10	217.9 ± 52.0^{a}	144.9–290.6	<0.001*
Placebo	10	$99,528.76 \pm 56,395.11^{b}$	16,136.30–186,255.76	
Steroid	10	$314,182.38 \pm 119,942.73^{c}$	135,804.19–483,868.47	
Nigella sativa L.	10	$229,322.63 \pm 54,432.00^{d}$	149,168.74–326,112.20	

*dsDNA: Kruskal-Wallis test, significant if $\alpha < 0.05$; a,b,c,d Superscript showed the significant difference between the treatment group (Mann-Whitney U test); IL17:Kruskal-Wallis test, significant if $\alpha < 0.05$; a,b,c,d Superscript showed the significant difference between the treatment group (Mann-Whitney U test); IL6:Kruskal-Wallis test, significant if $\alpha < 0.0$; a,b,c,d Superscript showed the significant difference between the treatment group (Mann-Whitney U test); IL23:OnewayAnova, significant if $\alpha < 0.05$; a,b,c Superscript showed the significant difference between treatment group of LSD multiple comparisons; Treg: Kruskal-Wallis test, significant if $p = 0.05$; a,b,c,d Superscript showed there is a significant difference among the treatment groups (multiple comparisons Games-Howell).

Table 3. Histopathological classification of LN, AI and CD34 cells in Healthy and Treatment groups.

Groups	n	Histopathological classification of LN (class)	p-value
		Median (min–max)	
Healthy	10	I (I–I)[a]	0.001*
Placebo	10	IV (IV–IV)[d]	
Steroid	10	III(II–IV)[c]	
Nigella sativa L.	10	II (II–III)[b]	
		AI	
		Median (min–max)	
Healthy	10	2 (0–3)[a]	0.001*
Placebo	10	4.5 (1–5)[d]	
Steroid	10	3 (2–4)[c]	
Nigella sativa L.	10	2 (1–3)[b]	
		CD34	
		Mean (min–max)	
Healthy	10	79.0 ± 9.94^{a}	0.003*
Placebo	10	46.0 ± 31.69^{d}	
Steroid	10	57.0 ± 18.88^{c}	
Nigella sativa L.	10	76.5 ± 10.55	

*Kruskal-Wallis test; groups identified using different letters (a,b,c,d) are statistically significant ($p < 0.05$, Mann-Whitney test); LN: Lupus Nephritis; AI: Activity Indices; NIH: National Institutes of Health.

5. Conclusion

Nigella sativa L. can be consumed as the complementary medication for SLE, it has been proved to modulate the immune system by reducing the expression of proinflammatory response cytokine (IL-6, IL-17, IL-23) and increasing the expression of Tregs significantly, *Nigella sativa* L. also can prevent renal tissue damage in PIL model. Further studies in humans are needed regarding the effects of *Nigella sativa* L. as an immunomodulator and prevention of kidney disease, and evaluation of the negative effects, especially in humans.

Declarations

Author contribution statement

Zahrah Hikmah: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Anang Endaryanto: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

I Dewa Gede Ugrasena: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Anny Setijo Rahaju: Analyzed and interpreted the data; Wrote the paper.

Syaiful Arifin: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Acknowledgements

We would like to thank and appreciate the support of our Colleague in Child Health of Department, Dr. Soetomo Academic Hospital/Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia.

References

Agustiarini, V., Darmawan, E., Akrom, A., 2019. The effects of dosage variation in black seed cumin oil (Nigella sativa L.) use on HbA1c levels and interleukin-17A expression in patients at risks of metabolic syndrome. Pharmaciana 9 (2), 10.

Ahmed, Z., Prawiro, S.R., Endharti, A.T., 2018. Nigella sativa extract increases antibacterial activity by up-regulating T-reg and Th2 levels in Salmonella enterica subsp. enterica serovars typhimurium-exposed balb/c mice. Res. J. Life Sci. 5 (1), 14–22.

Alchi, B., Jayne, D., Labopin, M., Kotova, O., Sergeevicheva, V., Alexander, T., Gualandi, F., Gruhn, B., Ouyang, J., Rzepecki, P., 2013. Autologous haematopoietic stem cell transplantation for systemic lupus erythematosus: data from the European Group for Blood and Marrow Transplantation registry. Lupus 22 (3), 245–253.

Amissah-Arthur, M.B., Gordon, C., 2010. Contemporary treatment of systemic lupus erythematosus: an update for clinicians. Ther. Adv. Chronic Dis. 1 (4), 163–175.

Arjumand, S., Shahzad, M., Shabbir, A., Yousaf, M.Z., 2019. Thymoquinone attenuates rheumatoid arthritis by downregulating TLR2, TLR4, TNF-α, IL-1, and NFκB expression levels. Biomed. Pharmacother. 111, 958–963.

Bajema, I.M., Wilhelmus, S., Alpers, C.E., Bruijn, J.A., Colvin, R.B., Cook, H.T., D'Agati, V.D., Ferrario, F., Haas, M., Jennette, J.C., 2018. Revision of the International Society of Nephrology/Renal Pathology Society classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices. Kidney Int. 93 (4), 789–796.

Barlianto, W., Kusuma, H.C., Widodo, M.A., Suharto, S., 2012. Crude extract of black seed (Nigella sativa) can modulate T CD4+ CD25+ FoxP3+ lymphocytes in asthmatic mouse model. Paediatr. Respir. Rev. (13), S54.

Crispín, J.C., Kyttaris, V.C., Terhorst, C., Tsokos, G.C., 2010. T cells as therapeutic targets in SLE. Nat. Rev. Rheumatol. 6 (6), 317–325.

Cunha, J.S., Gilek-Seibert, K., 2016. Systemic lupus erythematosus: a review of the clinical approach to diagnosis and update on current targeted therapies. R. I. Med. J. 99 (12), 23–27, 2013.

Dolff, S., Bijl, M., Huitema, M.G., Limburg, P.C., Kallenberg, C.G., Abdulahad, W.H., 2011. Disturbed Th1, Th2, Th17 and Treg balance in patients with systemic lupus erythematosus. Clin. Immunol. 141 (2), 197–204.

Faisal, R., Shinwari, L., Jehangir, T., 2015. Comparison of the therapeutic effects of thymoquinone and methotrexate on renal injury in pristane induced arthritis in rats. J. Coll. Physicians Surg. Pak. 25 (8), 597–601.

Farhangi, M.A., Dehghan, P., Tajmiri, S., Abbasi, M.M., 2016. The effects of Nigella sativa on thyroid function, serum Vascular Endothelial Growth Factor (VEGF)–1, Nesfatin-1 and anthropometric features in patients with Hashimoto's thyroiditis: a randomized controlled trial. BMC Compl. Alternative Med. 16 (1), 1–9.

Fava, A., Petri, M., 2019. Systemic lupus erythematosus: diagnosis and clinical management. J. Autoimmun. 96, 1–13.

Freitas, E.C., de Oliveira, M.S., Monticielo, O.A., 2017. Pristane-induced lupus: considerations on this experimental model. Clin. Rheumatol. 36 (11), 2403–2414.

Giraldo, W.A.S., Villanueva, M.J.G., Boteanu, A.L., Iglesias, A.L., Mendoza, A.C.Z., 2012. New therapeutic targets in systemic lupus. Reumatol. Clínica 8 (4), 201–207.

Hamijoyo, L., Candrianita, S., Rahmadi, A.R., Dewi, S., Darmawan, G., Suryajaya, B.S., Rainy, N.R., Hidayat II, Moenardi, V.N., Wachjudi, R.G., 2019. The clinical characteristics of systemic lupus erythematosus patients in Indonesia: a cohort registry from an Indonesia-based tertiary referral hospital. Lupus 28 (13), 1604–1609.

Hiraki, L.T., Benseler, S.M., Tyrrell, P.N., Hebert, D., Harvey, E., Silverman, E.D., 2008. Clinical and laboratory characteristics and long-term outcome of pediatric systemic lupus erythematosus: a longitudinal study. J. Pediatr. 152 (4), 550–556.

Hmza, A., Osman, M., Adnan, A., Omar, E., 2013. Immunomodulatory effect of Nigella sativa oil in the disease process of type 1 diabetic rats. Res. J. Pharmaceut. Biol. Chem. Sci. 4, 980–988.

Hossen, M.J., Yang, W.S., Kim, D., Aravinthan, A., Kim, J.-H., Cho, J.Y., 2017. Thymoquinone: an IRAK1 inhibitor with in vivo and in vitro anti-inflammatory activities. Sci. Rep. 7 (1), 1–12.

Islam, M.T., Guha, B., Hosen, S., Riaz, T.A., Shahadat, S., Da Rocha Sousa, L., De Oliveira Santos, J.V., Da Silva Júnior, J.J., De Lima, R.M.T., Braga, A.L., 2017. Nigellalogy: a review on Nigella sativa. MOJ Bioequiv. Availab. 3 (6), 00056.

Kabir, Y., Akasaka-Hashimoto, Y., Kubota, K., Komai, M., 2020. Volatile compounds of black cumin (Nigella sativa L.) seeds cultivated in Bangladesh and India. Heliyon 6 (10), e05343.

Kasturi, S., Sammaritano, L.R., 2016. Corticosteroids in lupus. Rheum. Dis. Clin. 42 (1), 47–62.

Kaul, A., Gordon, C., Crow, M.K., Touma, Z., Urowitz, M.B., van Vollenhoven, R., Ruiz-Irastorza, G., Hughes, G., 2016. Systemic lupus erythematosus. Nat. Rev. Dis. Prim. 2, 16039.

Kheirouri, S., Hadi, V., Alizadeh, M., 2016. Immunomodulatory effect of Nigella sativa oil on T lymphocytes in patients with rheumatoid arthritis. Immunol. Invest. 45 (4), 271–283.

Kudo, C., 2015. Major side effects of systemic glucocorticoid. Nihon rinsho. Jpn J. Clin. Med. 73 (2), 317–321.

La Paglia, G.M.C., Leone, M.C., Lepri, G., Vagelli, R., Valentini, E., Alunno, A., Tani, C., 2017. One year in review 2017: systemic lupus erythematosus. Clin. Exp. Rheumatol. 35 (4), 551–561.

Li, D., Guo, B., Wu, H., Tan, L., Chang, C., Lu, Q., 2015. Interleukin-17 in systemic lupus erythematosus: a comprehensive review. Autoimmunity 48 (6), 353–361.

Li, W., Titov, A.A., Morel, L., 2017. An update on lupus animal models. Curr. Opin. Rheumatol. 29 (5), 434.

Maitra, U., Davis, S., Reilly, C.M., Li, L., 2009. Differential regulation of Foxp3 and IL-17 expression in CD4 T helper cells by IRAK-1. J. Immunol. 182 (9), 5763–5769.

Oon, S., Huq, M., Godfrey, T., Nikpour, M., 2018. Systematic review, and meta-analysis of steroid-sparing effect, of biologic agents in randomized, placebo-controlled phase 3 trials for systemic lupus erythematosus. In: Seminars in Arthritis and Rheumatism. Elsevier, pp. 221–239.

Osio-Salido, E., Manapat-Reyes, H., 2010. Epidemiology of systemic lupus erythematosus in Asia. Lupus 19 (12), 1365–1373.

Pinheiro, S.V.B., Dias, R.F., Fabiano, R.C.G., Araujo, S.d.A., Silva, A.C.S.e., 2019. Pediatric lupus nephritis. Braz. J. Nephrol. 41 (2), 252–265.

Prastiwi, R., Iqbal, A., Kristi, A., 2015. Aktivitas imunomodulator ekstrak n-heksana, etil asetat, dan metanol Biji Jinten Hitam (Nigella sativa L.). Jurnal Farmasi Sains dan Terapan 2 (2).

Rönnblom, L., Elkon, K.B., 2010. Cytokines as therapeutic targets in SLE. Nat. Rev. Rheumatol. 6 (6), 339–347.

Sada, K.E., Makino, H., 2009. Usefulness of ISN/RPS classification of lupus nephritis. J. Kor. Med. Sci. 24 (Suppl 1), S7–10.

Salem, A.M., Bamosa, A.O., Qutub, H.O., Gupta, R.K., Badar, A., Elnour, A., Afzal, M.N., 2017. Effect of Nigella sativa supplementation on lung function and inflammatory mediators in partly controlled asthma: a randomized controlled trial. Ann. Saudi Med. 37 (1), 64–71.

Shahzad, M., Yang, X., Asim, M.R., Sun, Q., Han, Y., Zhang, F., Cao, Y., Lu, S., 2009. Black seed oil ameliorates allergic airway inflammation by inhibiting T-cell proliferation in rats. Pulm. Pharmacol. Therapeut. 22 (1), 37–43.

Shaterzadeh-Yazdi, H., Noorbakhsh, M.F., Hayati, F., Samarghandian, S., Farkhondeh, T., 2018a. Immunomodulatory and anti-inflammatory effects of thymoquinone. Cardiovasc. Haematol. Disord. - Drug Targets 18 (1), 52–60.

Shaterzadeh-Yazdi, H., Noorbakhsh, M.-F., Samarghandian, S., Farkhondeh, T., 2018b. An overview on renoprotective effects of Thymoquinone. Kidney Dis. 4 (2), 74–82.

Sinha, A., Bagga, A., 2008. Pulse steroid therapy. Indian J. Pediatr. 75 (10), 1057–1066.

Su, G., Luan, Z., Wu, F., Wang, X., Tang, X., Wu, N., Wang, K., 2013. Long-term follow-up of autologous stem cell transplantation for severe paediatric systemic lupus erythematosus. Clin. Rheumatol. 32 (12), 1727–1734.

Suprijono, A., Paramita, A., 2021. Pengaruh pemberian minyak jinten Hitam (Nigella sativa) terhadap indeks apoptosis adenokarsinoma mammae secara in vivo studi eksperimental mencit galur C3h yang diinokulasi sel adenokarsinoma mammae. Majalah Ilmiah Sultan Agung 50 (127), 13–22.

Susanti, N., Barlianto, W., Kalim, H., Kusuma, H.M.S.C., 2013. Asthma clinical improvement and reduction in the number of CD4+CD25+foxp3+Treg and CD4+IL-10+ cells after administration of immunotherapy house dust mite and adjuvant probiotics and/or Nigella sativa powder in mild asthmatic children. IOSR J. Dent. Med. Sci. 7, 50–59.

Tackey, E., Lipsky, P., Illei, G., 2004. Rationale for interleukin-6 blockade in systemic lupus erythematosus. Lupus 13 (5), 339–343.

Tajmiri, S., Farhangi, M.A., Dehghan, P., 2016. Nigella Sativa treatment and serum concentrations of thyroid hormones, transforming growth factor β (TGF-β) and interleukin 23 (IL-23) in patients with Hashimoto's Thyroiditis. Eur. J. Integr. Med. 8 (4), 576–580.

Umar, S., Zargan, J., Umar, K., Ahmad, S., Katiyar, C.K., Khan, H.A., 2012. Modulation of the oxidative stress and inflammatory cytokine response by thymoquinone in the collagen induced arthritis in Wistar rats. Chem. Biol. Interact. 197 (1), 40–46.

Wen, C.C., Chen, H.M., Yang, N.S., 2012. Developing phytocompounds from medicinal plants as immunomodulators. Adv. Bot. Res. 62, 197–272.

Yan, Y., Zhang, Z., Chen, Y., Hou, B., Liu, K., Qin, H., Fang, L., Du, G., 2020. Coptisine alleviates pristane-induced lupus-like disease and associated kidney and cardiovascular complications in mice. Front. Pharmacol. 11, 929.

Yap, D.Y.H., Lai, K.N., 2010. Cytokines and their roles in the pathogenesis of systemic lupus erythematosus: from basics to recent advances. J. Biomed. Biotechnol. 2010, 365083.

Heliyon

COUNTRY

Netherlands

Universities and research institutions in Netherlands

SUBJECT AREA AND CATEGORY

Multidisciplinary
Multidisciplinary

PUBLISHER

Elsevier BV

H-INDEX

46

PUBLICATION TYPE

Journals

ISSN

24058440

COVERAGE

2015-2021

INFORMATION

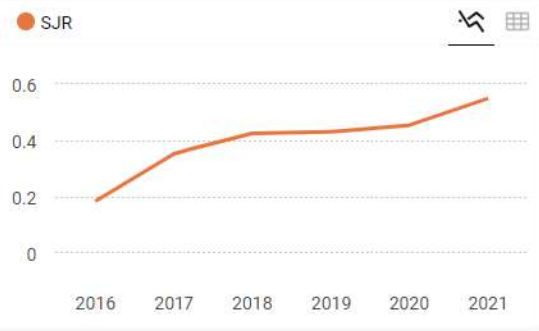
Homepage

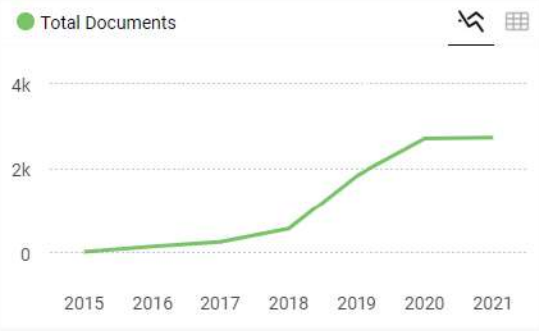
How to publish in this journal

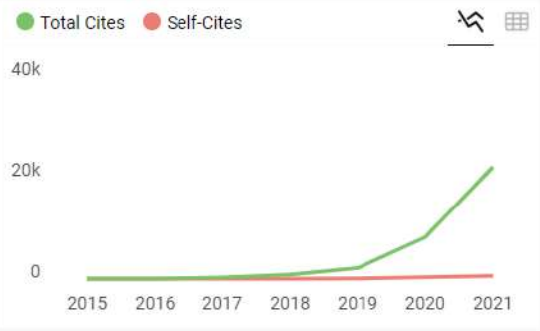
c.schulz@cell.com

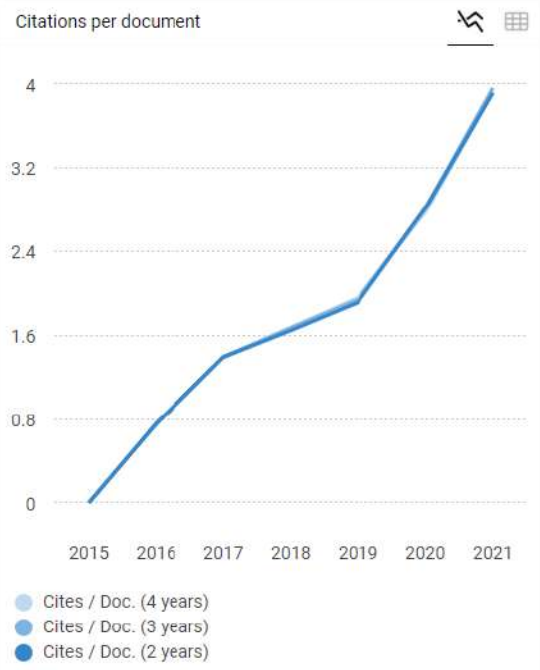
SCOPE

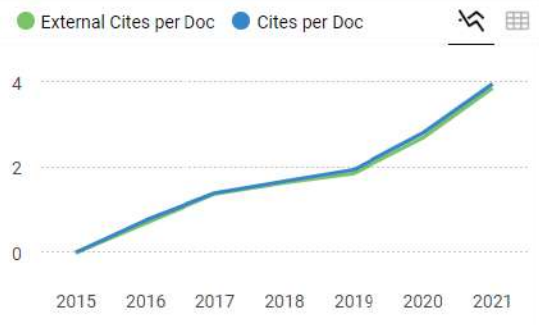
Heliyon is an all-science, open access journal that is part of the Cell Press family. Any paper reporting scientifically accurate and valuable research, which adheres to accepted ethical and scientific publishing standards, will be considered for publication. Our growing team of dedicated section editors, along with our in-house team, handle your paper and manage the publication process end-to-end, giving your research the editorial support it deserves.

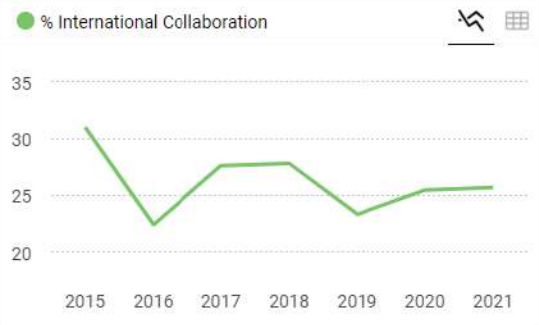


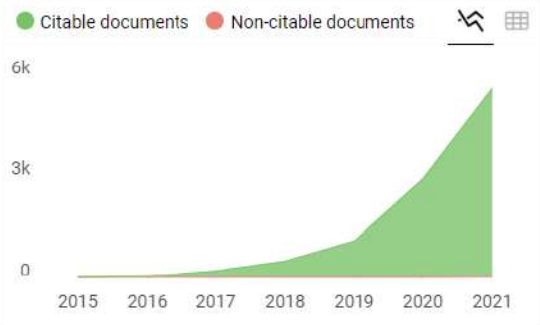


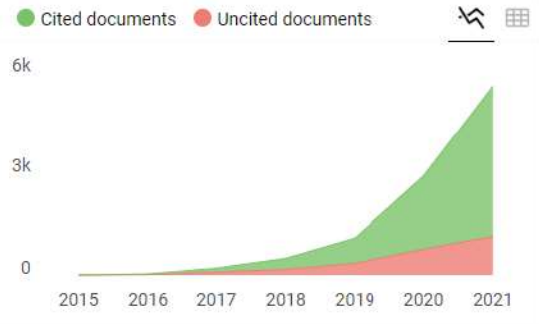












← Show this widget in your own website

Just copy the code below and paste within your html code:

```
<a href="https://www.scimag
```

SCImago Graphica

Explore, visually communicate and make sense of data with our **new data visualization tool**.

Source details

Heliyon

Open Access

Scopus coverage years: from 2015 to Present

Publisher: Elsevier

E-ISSN: 2405-8440

Subject area: Multidisciplinary

Source type: Journal

CiteScore 2021
4.0

SJR 2021
0.550

SNIP 2021
1.270

View all documents > | Set document alert | Save to source list | Source Homepage

CiteScore | CiteScore rank & trend | Scopus content coverage

¡ Improved CiteScore methodology

CiteScore 2021 counts the citations received in 2018-2021 to articles, reviews, conference papers, book chapters and data papers published in 2018-2021, and divides this by the number of publications published in 2018-2021. Learn more >

CiteScore 2021

$$4.0 = \frac{31{,}820 \text{ Citations } 2018 - 2021}{7{,}880 \text{ Documents } 2018 - 2021}$$

Calculated on 05 May, 2022

CiteScoreTracker 2022

$$5.2 = \frac{46{,}303 \text{ Citations to date}}{8{,}940 \text{ Documents to date}}$$

Last updated on 05 September, 2022 • Updated monthly

CiteScore rank 2021

Category	Rank	Percentile
Multidisciplinary └ Multidisciplinary	#22/120	82nd

View CiteScore methodology > | CiteScore FAQ > | Add CiteScore to your site

KOMISI ETIK PENELITIAN
FAKULTAS KEDOKTERAN HEWAN UNIVERSITAS AIRLANGGA
Animal Care and Use Committee (ACUC)

KETERANGAN KELAIKAN ETIK

" ETHICAL CLEARENCE"

No : 2.KE.165.08.2019

KOMISI ETIK PENELITIAN (*ANIMAL CARE AND USE COMMITTEE*) FAKULTAS KEDOKTERAN HEWAN UNIVERSITAS AIRLANGGA SURABAYA, TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA :

PENELITIAN BERJUDUL	: Mekanisme Penecgahan Progresivitas Lupus Eritematosus Sistemik Dengan Pemberian Ekstrak *Nigella sativa* pada Mencit Model Lupus
PENELITI UTAMA	: Zahrah Hikmah
UNIT/LEMBAGA/TEMPAT PENELITIAN	: Program Studi Ilmu Kedokteran Jenjang Doktor Fakultas Kedokteran Universitas Airlangga
DINYATAKAN	: LAIK ETIK

Surabaya, 15 Agustus 2019

Mengetahui,
Dekan FKH-Unair,

Prof. Dr. Pudji Srianto, M.Kes.,Drh.
NIP. 195601051986011001

Ketua,

Dr. Nusdianto Triakoso, M.P.,Drh.
NIP. 196805051997021001