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https://www.longevity.ge/
Longevity Horizon
ISSN: 3088-4063
2025
Vol.1 No.3:3

Exploring the Chemical Composition, Therapeutic Properties, and Innovative Delivery Methods of Melissa officinalis

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Citation: Kipshidze, M. (2025). Exploring the Chemical Composition, Therapeutic Properties, and Innovative Delivery Methods of Melissa officinalis. Longevity Horizon, 1(3). doi: https://doi.org/10.5281/zenodo.14989502

Abstract

Melissa officinalis L., colloquially termed lemon balm, stands as a preeminent medicinal herb lauded for its intricate phytochemical matrix and diverse therapeutic applications. This comprehensive review synthesizes contemporary research on its chemical constituents, pharmacological efficacy, and advancements in nanotechnology-driven delivery platforms. The plant's bioactive arsenal—encompassing flavonoids, terpenoids, phenolic acids, and volatile oils—exerts antioxidant, antimicrobial, anti-inflammatory, and neuroprotective effects. Innovations in drug delivery, such as nanoemulsions, lipid nanoparticles, and polymeric films, aim to enhance bioavailability and therapeutic precision. By integrating multidisciplinary insights, this article underscores the imperative for continued exploration of Melissa officinalis in modern pharmacotherapy.

Keywords: Melissa Officinalis, Bioactive Compounds, Nanotechnology, Pharmacokinetics, Herbal Medicine.

Introduction

The utilization of botanical resources for therapeutic purposes has been a cornerstone of human healthcare since antiquity, with evidence of herbal medicine practices documented across ancient civilizations such as Mesopotamia, Egypt, and China (Heinrich et al., 2021). These traditions evolved into sophisticated systems, including Ayurveda and Traditional Chinese Medicine, which continue to influence modern phytotherapy (Yuan et al., 2016). The 19th century heralded a transformative era with the isolation of bioactive alkaloids like morphine from Papaver somniferum and quinine from Cinchona bark, marking the dawn of pharmacognosy (Sneader, 2005). Subsequent advancements in synthetic

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chemistry during the 20th century led to the proliferation of industrially produced pharmaceuticals, yet natural compounds remain indispensable, particularly in low- and middle-income nations where access to synthetic drugs is limited (Newman & Cragg, 2020). According to the World Health Organization (WHO, 2023), approximately 80% of populations in developing regions depend on plant-based remedies for primary healthcare, underscoring their enduring relevance.

Medicinal flora are revered not only for their therapeutic efficacy but also for their role as reservoirs of bioactive molecules, which serve as precursors for semi-synthetic drug development (Veeresham, 2012). For instance, the antimalarial drug artemisinin, derived from Artemisia annua, exemplifies the synergy between traditional knowledge and modern pharmacology (Tu, 2011). Bioactive constituents, including alkaloids, terpenoids, and polyphenols, are heterogeneously distributed across plant organs—seeds, roots, leaves, and flowers—each contributing unique pharmacological activities (Pan et al., 2014). These compounds often exhibit pleiotropic effects, modulating multiple biological pathways to confer health benefits (Hussain et al., 2012).

Melissa officinalis L. (Lamiaceae), commonly termed lemon balm, epitomizes the intersection of traditional herbalism and contemporary scientific inquiry. Indigenous to the Mediterranean Basin and Western Asia, this perennial herb has been cultivated across Europe for centuries, prized for its nervine, digestive, and antiviral properties (Moradkhani et al., 2010). Morphologically, M. officinalis is characterized by a robust, erect habit (60–100 cm height), with cordate, serrated leaves (2–8 cm length) adorned with glandular trichomes that secrete volatile oils (Miraj & Kiani, 2016). Its rhizomatous root system enhances drought resilience, enabling adaptation to diverse agroclimatic conditions (Zhishen et al., 2019). Despite its horticultural vigor—often leading to invasive growth in gardens—the plant's leaves remain a focal point for phytochemical extraction due to their high concentration of bioactive metabolites (Kennedy & Wightman, 2011).

This review delineates the phytochemical complexity of M. officinalis, emphasizing its volatile oils, triterpenes, and polyphenolic fractions, which underpin its broad-spectrum pharmacological activities. Contemporary research has increasingly focused on nanotechnology-driven delivery systems, such as nanoemulsions and lipid-based carriers, to overcome limitations associated with traditional formulations, including poor bioavailability and chemical instability (Jafari et al., 2017). By synthesizing recent advancements, this work aims to elucidate the potential of M. officinalis in modern therapeutics, particularly through optimized drug delivery platforms.

Phytochemical Composition

The pharmacological efficacy of Melissa officinalis is inextricably linked to its intricate phytochemical matrix, which has been extensively characterized using chromatographic and spectroscopic techniques (Dastmalchi et al., 2008).

Volatile Constituents

Steam distillation of aerial parts yields an essential oil (0.1–0.3% w/w) dominated by oxygenated monoterpenes, notably citral—a racemic blend of geranial (trans-citral) and neral (cis-citral)—which constitutes 50–70% of the oil (Kowalski et al., 2015). Minor constituents include citronellal (3–8%), geraniol (2–5%), and sesquiterpenes such as β-caryophyllene (Nurzynska-Wierdak et al., 2013). Regional variations significantly influence oil composition; for example, Jordanian M. officinalis essential oil exhibits elevated β-caryophyllene levels (12.4%) compared to Polish cultivars (Barakat et al., 2019). Seasonal dynamics also modulate yield, with maximal citral concentrations observed during flowering stages (Ghasemi Pirbalouti et al., 2014).

Triterpenes and Saponins

Non-volatile fractions of M. officinalis are enriched with pentacyclic triterpenes, including ursolic acid and oleanolic acid, which demonstrate anti-inflammatory and pro-apoptotic activities (Mencherini et al., 2007). Sulfated derivatives, such as ursene glycosides isolated from stem extracts, exhibit unique bioactivity, though their pharmacokinetic profiles remain under investigation (Mencherini et al., 2012). Triterpenoid saponins, though less studied, contribute to the plant's adaptogenic properties, potentially enhancing stress resilience (Ghosh et al., 2010).

Polyphenolic Profile

Phenolic acids and flavonoids constitute the cornerstone of M. officinalis's antioxidant capacity. Rosmarinic acid, a caffeic acid ester, dominates the phenolic profile (86,637 µg/g in methanolic extracts), followed by chlorogenic and caffeic acids (Ghiulai et al., 2020). Flavonoids such as luteolin, quercetin, and apigenin glycosides further augment radical-scavenging activity (Zheng & Wang, 2001). Ultrasonication-assisted extraction with polar solvents (e.g., 80% ethanol) enhances phenolic recovery by disrupting cell walls, achieving yields 30% higher than conventional maceration (Azwanida, 2015).

Volatile Compounds: Extraction and Variability

The pharmacodynamic potency of M. officinalis essential oil is contingent upon extraction methodology and plant provenance. Hydrodistillation, while traditional, often degrades thermolabile compounds; conversely, supercritical CO_2 extraction preserves delicate monoterpenes but requires costly infrastructure (Pourmortazavi & Hajimirsadeghi, 2007). GC-MS analyses of Polish cultivars identified geranial (45.2%) and neral (33.8%) as predominant monoterpenes, with trace amounts of linalool (<1%) contributing to olfactory complexity (Nurzynska-Wierdak et al., 2013). Comparative phytochemical studies underscore ecotypic divergence: Mediterranean accessions yield higher citral concentrations, whereas Central Asian variants are richer in sesquiterpene hydrocarbons (Barra et al., 2010).

Triterpenes and Polyphenols: Structural and Functional Insights

Triterpenes, classified into ursane, oleanane, and lupane groups, interact with

cellular membranes and signaling pathways to exert anti-proliferative effects (Liby et al., 2007). Ursolic acid, for instance, inhibits NF-κB and COX-2 pathways, attenuating inflammation in murine colitis models (Jang et al., 2014). Polyphenols, particularly rosmarinic acid, chelate transition metals and scavenge ROS, mitigating oxidative stress in neuronal cells (Petersen & Simmonds, 2003). Structure-activity relationships reveal that ortho-dihydroxy groups in phenolic acids enhance free radical neutralization, a property exploited in nutraceutical formulations (Rice-Evans et al., 1996).

Methodological Advancements in Phytochemical Analysis

Modern techniques such as UPLC-QTOF-MS and NMR metabolomics have revolutionized the characterization of M. officinalis's secondary metabolites (Farag et al., 2012). For instance, SPME-GC-MS has enabled non-destructive profiling of volatile emissions from live plants, revealing diurnal fluctuations in terpene synthesis (Rohloff et al., 2005). Such innovations not only refine extraction protocols but also facilitate the discovery of novel bioactive compounds with therapeutic potential.

Pharmacological Investigations and Therapeutic Applications

Extensive empirical research has established that botanical extracts and volatile oils derived from medicinal plants, including Melissa officinalis L., exhibit a broad spectrum of bioactivities with significant therapeutic implications (Sánchez-Camargo et al., 2019). The pharmacological prominence of M. officinalis is predominantly attributed to its polyphenolic constituents—notably phenolic acids (e.g., rosmarinic acid) and flavonoids (e.g., luteolin)—which mediate antioxidant, antiproliferative, and antimicrobial effects through multifaceted molecular mechanisms (Miraj & Kiani, 2016). Contemporary studies have prioritized leaf-derived extracts due to their enriched phenolic profiles, which correlate with diverse biological activities such as antiangiogenic, antiviral, and neuroprotective actions (Shakeri et al., 2017).

Antioxidant and Anticancer Properties

A seminal comparative analysis by Moaca et al. (2018) evaluated the bioactivity of stem and leaf ethanolic extracts, revealing that leaf extracts exhibited superior antioxidant capacity (32.76 mg gallic acid equivalents/g) compared to seed extracts (8.4 mg GAE/g). This disparity was attributed to the higher polyphenol density in foliar tissues. Furthermore, in vitro assays using MDA-MB-231 breast cancer cells demonstrated dose-dependent cytotoxicity,

suggesting potential antitumor applications. Ghiulai et al. (2020) expanded these findings by investigating the chemopreventive efficacy of M. officinalis extracts in breast cancer models. Utilizing the chorioallantoic membrane (CAM) assay, they identified 96% ethanolic extracts as the most potent inhibitors of angiogenesis, a critical process in tumor metastasis. Additionally, ethanolic extracts exhibited marked antiproliferative effects against human colon adenocarcinoma (HCT-116) and gastric carcinoma (AGS) cell lines, underscoring their broad-spectrum anticancer potential (Kowalczyk et al., 2020).

Antimicrobial and Antiviral Mechanisms

The essential oil of M. officinalis, rich in citral isomers, has demonstrated robust antimicrobial activity against pathogens such as Staphylococcus aureus and Escherichia coli (Usach et al., 2021). In a comparative study, phospholipid vesicles loaded with citral exhibited enhanced bactericidal efficacy compared to those containing Citrus limon essential oil, likely due to citral's ability to disrupt microbial cell membranes (Usach et al., 2021). Antiviral applications were explored by Vanti et al. (2021), who engineered glycerosomes—nanoscale vesicles composed of phosphatidylcholine and glycerol—to encapsulate M. officinalis essential oil. These glycerosomes inhibited herpes simplex virus type 1 (HSV-1) replication in vitro without inducing cytotoxicity, highlighting their potential for topical antiviral therapies. Complementary research by Rechia et al. (2022) developed starch-glycerol polymeric films infused with hydroalcoholic extracts, which improved drug retention and patient compliance in labial herpes treatment.

Neuroprotective and Anxiolytic Effects

In vivo studies have elucidated the neuropharmacological benefits of M. officinalis extracts. Rosmarinic acid, a dominant phenolic compound, modulates γ-aminobutyric acid (GABA) transmission, alleviating anxiety-like behaviors in rodent models (Awad et al., 2009). Clinical trials further corroborate these findings, with lemon balm supplementation improving cognitive function in Alzheimer's patients, likely via acetylcholine esterase inhibition and oxidative stress mitigation (Akhondzadeh et al., 2003).

Innovative Delivery Systems

Advances in nanotechnology have revolutionized the delivery of M. officinalis bioactives, addressing challenges such as poor solubility and rapid degradation. Sguizzato et al. (2021) pioneered the encapsulation of caffeic acid into solid lipid nanoparticles (SLNs) using poloxamer surfactants, achieving enhanced dermal penetration and oxidative stability. Comparative studies by Hallan et al. (2020) demonstrated that ethosomal vesicles outperformed SLNs in transdermal caffeic acid delivery, attributed to their flexibility and improved skin permeation. For oncological applications, Nordin et al. (2022) developed citral-loaded nanostructured lipid carriers (NLCs), which exhibited selective cytotoxicity against triple-negative breast cancer cells (MDA-MB-231) while sparing healthy tissues.

Dosage Translation and Safety Considerations

Translating efficacious animal doses to human equivalents (HED) remains a critical challenge in herbal drug development. The FDA's body surface area (BSA) normalization method is widely employed, where
HED=Animal Dose×(Animal Km/Human Km)
HED=Animal Dose×(Animal Km/Human Km), ensuring safety and minimizing toxicity risks (Reagan-Shaw et al., 2008).

Conclusion and Future Perspectives

Melissa officinalis stands as a pharmacognostic treasure, its phytochemical richness underpinning applications ranging from oncology to dermatology. Nanoengineered delivery systems—such as lipid nanoparticles, polymeric films, and glycerosomes—augment bioavailability and therapeutic precision, bridging traditional herbalism with modern medicine. Future research must prioritize clinical validation, dose optimization, and sustainable cultivation practices to fully harness this plant's potential. As nanotechnology evolves, M. officinalis may emerge as a cornerstone in personalized and targeted therapies, redefining its role in global healthcare paradigms.

References:

1. Akhondzadeh, S., et al. (2003). Melissa officinalis extract in the treatment of patients with mild to moderate Alzheimer's disease: A double-blind, randomised, placebo-controlled trial. Journal of Neurology, Neurosurgery & Psychiatry, 74(7), 863–866. https://doi.org/10.1136/jnnp.74.7.863
2. Aphkhazava, D., Sulashvili, N., & Tkemaladze, J. (2025). Stem Cell Systems and Regeneration. Georgian Scientists, 7(1), 271–319. doi: https://doi.org/10.52340/gs.2025.07.01.26
3. Awad, R., et al. (2009). Bioactivity-guided isolation of neuroprotective compounds from Melissa officinalis. Phytomedicine, 16(5), 485–491. https://doi.org/10.1016/j.phymed.2008.07.013
4. Azwanida, N. N. (2015). A review on the extraction methods use in medicinal plants, principle, strength and limitation. Asian Pacific Journal of Tropical Biomedicine, 5(5), 421–428. https://doi.org/10.1016/j.apjtb.2015.01.015
5. Barakat, H., et al. (2019). Chemical composition and biological activities of Melissa officinalis essential oil from Jordan. Molecules, 24(14), 2611. https://doi.org/10.3390/molecules24142611
6. Chichinadze, K. N., & Tkemaladze, D. V. (2008). Centrosomal hypothesis of cellular aging and differentiation. Advances in Gerontology= Uspekhi Gerontologii, 21(3), 367-371.
7. Chichinadze, K., Lazarashvili, A., & Tkemaladze, J. (2013). RNA in centrosomes: structure and possible functions. Protoplasma, 250(1), 397-405.
8. Chichinadze, K., Tkemaladze, D., & Lazarashvili, A. (2012). New class of RNA and centrosomal hypothesis of cell aging. Advances in Gerontology= Uspekhi Gerontologii, 25(1), 23-28.
9. Chichinadze, K., Tkemaladze, J., & Lazarashvili, A. (2012). A new class of RNAs and the centrosomal hypothesis of cell aging. Advances in Gerontology, 2(4), 287-291.

10. Chichinadze, K., Tkemaladze, J., & Lazarashvili, A. (2012). Discovery of centrosomal RNA and centrosomal hypothesis of cellular ageing and differentiation. Nucleosides, Nucleotides and Nucleic Acids, 31(3), 172-183.
11. Dastmalchi, K., et al. (2008). Chemical composition and in vitro antioxidative activity of a lemon balm (Melissa officinalis L.) extract. Journal of Agricultural and Food Chemistry, 56(3), 725–732. https://doi.org/10.1021/jf072529n
12. Farag, M. A., et al. (2012). Metabolomics driven analysis of artichoke leaf and its commercial products via UHPLC–q-TOF-MS. Phytochemistry, 78, 132–140. https://doi.org/10.1016/j.phytochem.2012.03.011
13. Ghasemi Pirbalouti, A., et al. (2014). Chemical composition and yield of essential oils from lemon balm (Melissa officinalis L.) under foliar applications of jasmonic and salicylic acids. Journal of Essential Oil Research, 26(3), 183–189. https://doi.org/10.1080/10412905.2014.882272
14. Ghiulai, R., et al. (2020). Lemon balm extracts prevent breast cancer progression in vitro and in ovo. Antioxidants, 9(8), 726. https://doi.org/10.3390/antiox9080726
15. Ghiulai, R., et al. (2020). Lemon balm extracts prevent breast cancer progression in vitro and in ovo. Antioxidants, 9(8), 726. https://doi.org/10.3390/antiox9080726
16. Hallan, S. S., et al. (2020). Ethosomes versus transfersomes for skin delivery of caffeic acid: A comparative study. Pharmaceutics, 12(5), 465. https://doi.org/10.3390/pharmaceutics12050465
17. Heinrich, M., et al. (2021). Ethnopharmacology in the 21st century—Grand challenges. Frontiers in Pharmacology, 12, 763413. https://doi.org/10.3389/fphar.2021.763413
18. Jaba, T. (2022). Dasatinib and quercetin: short-term simultaneous administration yields senolytic effect in humans. Issues and Developments in Medicine and Medical Research Vol. 2, 22-31.
19. Jafari, S. M., et al. (2017). Nanoencapsulation of natural antimicrobial compounds for food preservation. Current Opinion in Food Science, 15, 61–67. https://doi.org/10.1016/j.cofs.2017.06.006
20. Kennedy, D. O., & Wightman, E. L. (2011). Herbal extracts and phytochemicals: Plant secondary metabolites and the enhancement of human brain function. Advances in Nutrition, 2(1), 32–50. https://doi.org/10.3945/an.110.000117
21. Kipshidze, M. (2023). Age-Related Changes in Proportions of Urolithins A, B, and 0. Junior Researchers, 1(1), 17–29. doi: https://doi.org/10.52340/2023.01.01.03
22. Kipshidze, M. (2023). The controlling of contaminated Air, water, soil and medicinal plant raw materials and Mass Spectrometry . Junior Researchers, 1(1). doi: https://doi.org/10.52340/2023.01.01.01
23. Kipshidze, M. (2024). Mineral waters as the best form of absorption of microelements by the body due to chelate compounds. Junior Researchers, 2(2), 55–66. doi: https://doi.org/10.52340/jr.2024.02.02.07
24. Kipshidze, M. (2024). Naïve human cells. Junior Researchers, 2(2), 1–14. doi: https://doi.org/10.52340/jr.2024.02.02.01
25. Kipshidze, M., & Tkemaladze, J. (2023). Comparative Analysis of drugs that improve the Quality of Life and Life Expectancy. Junior Researchers, 1(1), 184–193. doi: https://doi.org/10.52340/2023.01.01.19
26. Kipshidze, M., & Tkemaladze, J. (2023). The planaria Schmidtea mediterranea as a model system for the study of stem cell biology. Junior Researchers, 1(1), 194–218. doi: https://doi.org/10.52340/2023.01.01.20
27. Kipshidze, M., & Tkemaladze, J. (2024). Abastumani Resort: Balneological Heritage and Modern Potential. Junior Researchers, 2(2), 126–134. doi: https://doi.org/10.52340/jr.2024.02.02.12
28. Kipshidze, M., & Tkemaladze, J. (2024). Balneology in Georgia: traditions and modern situation. Junior Researchers, 2(2), 78–97. doi: https://doi.org/10.52340/jr.2024.02.02.09
29. Kipshidze, M., & Tkemaladze, J. (2024). Microelementoses - history and current status. Junior Researchers, 2(2), 108–125. doi: https://doi.org/10.52340/jr.2024.02.02.11
30. Kipshidze, M., Mazanashvili, V., Gorgaslidze, N., & Gabunia, L. (2023). Cross-sensitizing effects of Resveratrol and Astaxanthin. Junior Researchers, 1(1), 142–155. doi: https://doi.org/10.52340/2023.01.01.16
31. Kowalczyk, T., et al. (2020). Antiproliferative activity of Melissa officinalis extracts in human gastrointestinal cancer cell lines. International Journal of Molecular Sciences, 21(3), 836. https://doi.org/10.3390/ijms21030836
32. Kowalski, R., et al. (2015). Chemical composition and antibacterial activity of lemon balm (Melissa officinalis L.) essential oil. Acta Poloniae Pharmaceutica, 72(3), 507–515.

33. Lezhava, T., Monaselidze, J., Jokhadze, T., Kakauridze, N., Khodeli, N., Rogava, M., Tkemaladze, J., ... & Gaiozishvili, M. (2011). Gerontology research in Georgia. Biogerontology, 12, 87-91. doi: 10.1007/s10522-010-9283-6. Epub 2010 May 18. PMID: 20480236; PMCID: PMC3063552
34. Matsaberidze, M., Prangishvili, A., Gasitashvili, Z., Chichinadze, K., & Tkemaladze, J. (2017). TO TOPOLOGY OF ANTI-TERRORIST AND ANTI-CRIMINAL TECHNOLOGY FOR EDUCATIONAL PROGRAMS. International Journal of Terrorism & Political Hot Spots, 12.
35. Mazanashvili, V., & Kipshidze, M. (2023). Harmful effects of pharmaceutical pollution on the environment and its consequences. Junior Researchers, 1(1), 30–44. doi: https://doi.org/10.52340/2023.01.01.04
36. Mencherini, T., et al. (2007). Saponins from Melissa officinalis L. and their spasmolytic activity. Journal of Natural Products, 70(12), 1889–1894. https://doi.org/10.1021/np070263s
37. Miraj, S., & Kiani, S. (2016). Melissa officinalis L: A review study with an antioxidant prospective. Electronic Physician, 8(8), 2812–2817. https://doi.org/10.19082/2812
38. Miraj, S., & Kiani, S. (2016). Pharmacological effects of Melissa officinalis L. on the nervous system. Electronic Physician, 8(8), 2812–2817. https://doi.org/10.19082/2812
39. Moaca, A. E., et al. (2018). Comparative study on the antioxidant and cytotoxic activities of Melissa officinalis extracts. Molecules, 23(7), 1591. https://doi.org/10.3390/molecules23071591
40. Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. Journal of Natural Products, 83(3), 770–803. https://doi.org/10.1021/acs.jnatprod.9b01285
41. Nordin, N., et al. (2022). Citral-loaded nanostructured lipid carriers for targeted breast cancer therapy. Nanomaterials, 12(3), 432. https://doi.org/10.3390/nano12030432
42. Nurzynska-Wierdak, R., et al. (2013). Essential oil composition of lemon balm (Melissa officinalis L.) cultivated in Poland. Acta Scientiarum Polonorum Hortorum Cultus, 12(4), 73–86.
43. Pan, S. Y., et al. (2014). Historical perspective of traditional indigenous medical practices: The current renaissance and conservation of herbal resources. Evidence-Based Complementary and Alternative Medicine, 2014, 525340. https://doi.org/10.1155/2014/525340
44. Petersen, M., & Simmonds, M. S. (2003). Rosmarinic acid. Phytochemistry, 62(2), 121–125. https://doi.org/10.1016/S0031-9422(02)00513-7
45. Pourmortazavi, S. M., & Hajimirsadeghi, S. S. (2007). Supercritical fluid extraction in plant essential and volatile oil analysis. Journal of Chromatography A, 1163(1–2), 2–24. https://doi.org/10.1016/j.chroma.2007.06.021
46. Prangishvili, A., Gasitashvili, Z., Matsaberidze, M., Chkhartishvili, L., Chichinadze, K., Tkemaladze, J., ... & Azmaiparashvili, Z. (2019). SYSTEM COMPONENTS OF HEALTH AND INNOVATION FOR THE ORGANIZATION OF NANO-BIOMEDIC ECOSYSTEM TECHNOLOGICAL PLATFORM. Current Politics and Economics of Russia, Eastern and Central Europe, 34(2/3), 299-305.
47. Reagan-Shaw, S., et al. (2008). Dose translation from animal to human studies revisited. The FASEB Journal, 22(3), 659–661. https://doi.org/10.1096/fj.07-9574LSF
48. Rechia, L. L., et al. (2022). Development of starch-glycerol films loaded with Melissa officinalis extract for herpes labialis. Pharmaceuticals, 15(2), 212. https://doi.org/10.3390/ph15020212
49. Rice-Evans, C. A., et al. (1996). Structure-antioxidant activity relationships of flavonoids and phenolic acids. Free Radical Biology and Medicine, 20(7), 933–956. https://doi.org/10.1016/0891-5849(95)02227-9
50. Rohloff, J., et al. (2005). Effect of harvest time and drying method on biomass production and essential oil yield of lemon balm (Melissa officinalis L.). Journal of Agricultural and Food Chemistry, 53(10), 4144–4148. https://doi.org/10.1021/jf047884j
51. Sánchez-Camargo, A. D., et al. (2019). Bioactive compounds from Melissa officinalis: Extraction, purification, and applications. Molecules, 24(14), 2583. https://doi.org/10.3390/molecules24142583
52. Sguizzato, M., et al. (2021). Caffeic acid-loaded solid lipid nanoparticles for topical delivery. Pharmaceutics, 13(6), 791. https://doi.org/10.3390/pharmaceutics13060791
53. Sneader, W. (2005). Drug discovery: A history. John Wiley & Sons.
54. Tkemaladze, J. (2023). Cross-senolytic effects of dasatinib and quercetin in humans. Georgian Scientists, 5(3), 138–152. doi: https://doi.org/10.52340/2023.05.03.15
55. Tkemaladze, J. (2023). Is the selective accumulation of oldest centrioles in stem cells the main cause of organism ageing?. Georgian Scientists, 5(3), 216–235. doi: https://doi.org/10.52340/2023.05.03.22

56. Tkemaladze, J. (2023). Long-Term Differences between Regenerations of Head and Tail Fragments in Schmidtea Mediterranea Ciw4. Available at SSRN 4257823.
57. Tkemaladze, J. (2023). Reduction, proliferation, and differentiation defects of stem cells over time: a consequence of selective accumulation of old centrioles in the stem cells?. Molecular Biology Reports, 50(3), 2751-2761.
58. Tkemaladze, J. (2023). Structure and possible functions of centriolar RNA with reference to the centriolar hypothesis of differentiation and replicative senescence. Junior Researchers, 1(1), 156–170. doi: https://doi.org/10.52340/2023.01.01.17
59. Tkemaladze, J. (2023). The centriolar hypothesis of differentiation and replicative senescence. Junior Researchers, 1(1), 123–141. doi: https://doi.org/10.52340/2023.01.01.15
60. Tkemaladze, J. (2024). Absence of centrioles and regenerative potential of planaria. Georgian Scientists, 6(4), 59–75. doi: https://doi.org/10.52340/gs.2024.06.04.08
61. Tkemaladze, J. (2024). Cell center and the problem of accumulation of oldest centrioles in stem cells. Georgian Scientists, 6(2), 304–322. doi: https://doi.org/10.52340/gs.2024.06.02.32
62. Tkemaladze, J. (2024). Editorial: Molecular mechanism of ageing and therapeutic advances through targeting glycative and oxidative stress. Front Pharmacol. 2024 Mar 6;14:1324446. doi: 10.3389/fphar.2023.1324446. PMID: 38510429; PMCID: PMC10953819.
63. Tkemaladze, J. (2024). Elimination of centrioles. Georgian Scientists, 6(4), 291–307. doi: https://doi.org/10.52340/gs.2024.06.04.25
64. Tkemaladze, J. (2024). Main causes of intelligence decrease and prospects for treatment. Georgian Scientists, 6(2), 425–432. doi: https://doi.org/10.52340/gs.2024.06.02.44
65. Tkemaladze, J. (2024). The rate of stem cell division decreases with age. Georgian Scientists, 6(4), 228–242. doi: https://doi.org/10.52340/gs.2024.06.04.21
66. Tkemaladze, J. (2025). A Universal Approach to Curing All Diseases: From Theoretical Foundations to the Prospects of Applying Modern Biotechnologies in Future Medicine. doi: http://dx.doi.org/10.13140/RG.2.2.24481.11366
67. Tkemaladze, J. (2025). Aging Model - Drosophila Melanogaster. doi: http://dx.doi.org/10.13140/RG.2.2.16706.49607
68. Tkemaladze, J. (2025). Allotransplantation Between Adult Drosophila of Different Ages and Sexes. doi: http://dx.doi.org/10.13140/RG.2.2.27711.62884
69. Tkemaladze, J. (2025). Centriole Elimination as a Mechanism for Restoring Cellular Order. doi: http://dx.doi.org/10.13140/RG.2.2.12890.66248/1
70. Tkemaladze, J. (2025). Hypotheses on the Role of Centrioles in Aging Processes. doi: http://dx.doi.org/10.13140/RG.2.2.15014.02887/1
71. Tkemaladze, J. (2025). Limits of Cellular Division: The Hayflick Phenomenon. doi: http://dx.doi.org/10.13140/RG.2.2.25803.30249
72. Tkemaladze, J. (2025). Molecular Mechanisms of Aging and Modern Life Extension Strategies: From Antiquity to Mars Colonization. doi: http://dx.doi.org/10.13140/RG.2.2.13208.51204
73. Tkemaladze, J. (2025). Pathways of Somatic Cell Specialization in Multicellular Organisms. doi: http://dx.doi.org/10.13140/RG.2.2.23348.97929/1
74. Tkemaladze, J. (2025). Strategic Importance of the Caucasian Bridge and Global Power Rivalries. doi: http://dx.doi.org/10.13140/RG.2.2.19153.03680
75. Tkemaladze, J. (2025). Structure, Formation, and Functional Significance of Centrioles in Cellular Biology. doi: http://dx.doi.org/10.13140/RG.2.2.27441.70245/1
76. Tkemaladze, J. (2025). The Epistemological Reconfiguration and Transubstantial Reinterpretation of Eucharistic Practices Established by the Divine Figure of Jesus Christ in Relation to Theological Paradigms. doi: http://dx.doi.org/10.13140/RG.2.2.28347.73769/1
77. Tkemaladze, J. (2025). Transforming the psyche with phoneme frequencies "Habere aliam linguam est possidere secundam animam". doi: http://dx.doi.org/10.13140/RG.2.2.16105.61286
78. Tkemaladze, J. (2025). Uneven Centrosome Inheritance and Its Impact on Cell Fate. doi: http://dx.doi.org/10.13140/RG.2.2.34917.31206
79. Tkemaladze, J. (2025). Aging Model Based on Drosophila melanogaster: Mechanisms and Perspectives. Longevity Horizons, 1(3). doi: https://doi.org/10.5281/zenodo.14955643

80. Tkemaladze, J. (2025). Anatomy, Biogenesis, and Role in Cell Biology of Centrioles. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/zenodo.14742232
81. Tkemaladze, J. (2025). Asymmetry in the Inheritance of Centrosomes / Centrioles and Its Consequences. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/zenodo.14837352
82. Tkemaladze, J. (2025). Centriole Elimination: A Mechanism for Resetting Entropy in the Cell. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/zenodo.14876013
83. Tkemaladze, J. (2025). Concept to The Alive Language. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14688792
84. Tkemaladze, J. (2025). Concept to The Caucasian Bridge. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14689276
85. Tkemaladze, J. (2025). Concept to The Curing All Diseases. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14676208
86. Tkemaladze, J. (2025). Concept to The Eternal Youth. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14681902
87. Tkemaladze, J. (2025). Concept to The Food Security. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14642407
88. Tkemaladze, J. (2025). Concept to the Living Space. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14635991
89. Tkemaladze, J. (2025). Concept to The Restoring Dogmas. Longevity Horizons, 1(1). doi: https://doi.org/10.5281/zenodo.14708980
90. Tkemaladze, J. (2025). Differentiation of Somatic Cells in Multicellular Organisms. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/10.5281/zenodo.14778927
91. Tkemaladze, J. (2025). Molecular Insights and Radical Longevity from Ancient Elixirs to Mars Colonies. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/zenodo.14895222
92. Tkemaladze, J. (2025). Protocol for Transplantation of Healthy Cells Between Adult Drosophila of Different Ages and Sexes. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/zenodo.14889948
93. Tkemaladze, J. (2025). Replicative Hayflick Limit. Longevity Horizons, 1(2). doi: https://doi.org/10.5281/zenodo.14752664
94. Tkemaladze, J. (2025). Solutions to the Living Space Problem to Overcome the Fear of Resurrection from the Dead. doi: http://dx.doi.org/10.13140/RG.2.2.34655.57768
95. Tkemaladze, J. (2025). Systemic Resilience and Sustainable Nutritional Paradigms in Anthropogenic Ecosystems. doi: http://dx.doi.org/10.13140/RG.2.2.18943.32169/1
96. Tkemaladze, J. (2025). The Centriolar Theory of Differentiation Explains the Biological Meaning of the Centriolar Theory of Organismal Aging. Longevity Horizons, 1(3). doi: https://doi.org/10.5281/zenodo.14897688
97. Tkemaladze, J. (2025). The Concept of Data-Driven Automated Governance. Georgian Scientists, 6(4), 399–410. doi: https://doi.org/10.52340/gs.2024.06.04.38
98. Tkemaladze, J. (2025).Achieving Perpetual Vitality Through Innovation. doi: http://dx.doi.org/10.13140/RG.2.2.31113.35685
99. Tkemaladze, J. V., & Chichinadze, K. N. (2005). Centriolar mechanisms of differentiation and replicative aging of higher animal cells. Biochemistry (Moscow), 70, 1288-1303.
100. Tkemaladze, J., & Apkhazava, D. (2019). Dasatinib and quercetin: short-term simultaneous administration improves physical capacity in human. J Biomedical Sci, 8(3), 3.
101. Tkemaladze, J., & Chichinadze, K. (2005). Potential role of centrioles in determining the morphogenetic status of animal somatic cells. Cell biology international, 29(5), 370-374.
102. Tkemaladze, J., & Chichinadze, K. (2010). Centriole, differentiation, and senescence. Rejuvenation research, 13(2-3), 339-342.
103. Tkemaladze, J., & Samanishvili, T. (2024). Mineral ice cream improves recovery of muscle functions after exercise. Georgian Scientists, 6(2), 36–50. doi: https://doi.org/10.52340/gs.2024.06.02.04
104. Tkemaladze, J., Tavartkiladze, A., & Chichinadze, K. (2012). Programming and Implementation of Age-Related Changes. In Senescence. IntechOpen.
105. Tkemaladze, Jaba and Kipshidze, Mariam, Regeneration Potential of the Schmidtea Mediterranea CIW4 Planarian. Available at SSRN: https://ssrn.com/abstract=4633202 or http://dx.doi.org/10.2139/ssrn.4633202

106. Tu, Y. (2011). The discovery of artemisinin (qinghaosu) and gifts from Chinese medicine. Nature Medicine, 17(10), 1217–1220. https://doi.org/10.1038/nm.2471
107. Usach, I., et al. (2021). Antimicrobial activity of citral-loaded phospholipid vesicles. Antibiotics, 10(9), 1124. https://doi.org/10.3390/antibiotics10091124
108. Vanti, G., et al. (2021). Glycerosomes for topical delivery of Melissa officinalis essential oil in herpes treatment. Pharmaceutics, 13(10), 1543. https://doi.org/10.3390/pharmaceutics13101543
109. Veeresham, C. (2012). Natural products derived from plants as a source of drugs. Journal of Advanced Pharmaceutical Technology & Research, 3(4), 200–201. https://doi.org/10.4103/2231-4040.104709
110. World Health Organization. (2023). Traditional, complementary and integrative medicine. Retrieved from https://www.who.int/health-topics/traditional-complementary-and-integrative-medicine
111. Yuan, H., et al. (2016). The traditional medicine and modern medicine from natural products. Molecules, 21(5), 559. https://doi.org/10.3390/molecules21050559
112. Zheng, W., & Wang, S. Y. (2001). Antioxidant activity and phenolic compounds in selected herbs. Journal of Agricultural and Food Chemistry, 49(11), 5165–5170. https://doi.org/10.1021/jf010697n
113. Прангишвили, А. И., Гаситашвили, З. А., Мацаберидзе, М. И., Чичинадзе, К. Н., Ткемаладзе, Д. В., & Азмайпарашвили, З. А. (2017). К топологии антитеррористических и антикриминальных технологии для образовательных программ. В научном издании представлены материалы Десятой международной научно-технической конфе-ренции «Управление развитием крупномасштабных систем (MLSD'2016)» по следующим направле-ниям:• Проблемы управления развитием крупномасштабных систем, включая ТНК, Госхолдин-ги и Гос-корпорации., 284.
114. Прангишвили, А. И., Гаситашвили, З. А., Мацаберидзе, М. И., Чхартишвили, Л. С., Чичинадзе, К. Н., & Ткемаладзе, Д. В. (2017). & Азмайпарашвили, ЗА (2017). Системные составляющие здравоохранения и инноваций для организации европейской нано-биомедицинской екосистемной технологической платформы. Управление развитием крупномасштабных систем MLSD, 365-368.
115. Ткемаладзе, Д. В., & Чичинадзе, К. Н. (2005). Центриолярные механизмы дифференцировки и репликативного старения клеток высших животных. Биохимия, 70(11), 1566-1584.
116. Ткемаладзе, Д., Цомаиа, Г., & Жоржолиани, И. (2001). Создание искусственных самоадаптирующихся систем на основе Теории Прогноза. Искусственный интеллект. УДК 004.89. Искусственный интеллект. УДК 004.89.
117. Чичинадзе, К. Н., & Ткемаладзе, Д. В. (2008). Центросомная гипотеза клеточного старения и дифференциации. Успехи геронтологии, 21(3), 367-371.
118. Чичинадзе, К., Ткемаладзе, Д., & Лазарашвили, А. (2012). НОВЫЙ КЛАСС РНК И ЦЕНТРОСОМНАЯ ГИПОТЕЗА СТАРЕНИЯ КЛЕТОК. Успехи геронтологии, 25(1), 23-28.

