KAROŃ, Karolina, KAROŃ, Łukasz, ZYGMUNT, Anna, GRABOWSKI, Wojciech, PEDRYCZ, Emilia, DRAPAŁA, Grzegorz and PEDRYCZ, Daria. Aromatic Serenity: How Lavender Eases Stress and Anxiety - A Literature Review. Quality in Sport. 2024;33:55778. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.33.55778
https://apcz.umk.pl/QS/article/view/55778

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assig589 ned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 23.10.2024. Revised: 13.11.2024. Accepted: 16.11.2024. Published: 16.11.2024.

Aromatic Serenity: How Lavender Eases Stress and Anxiety - A Literature Review

1. Karolina Karoń
   - affiliation: Municipal Hospital in Zabrze
   - ORCID: 0009-0005-0356-8907
   - corresponding author: e-mail: kkaron045@gmail.com
2. Łukasz Karoń
   - affiliation: Department of Pathology and Molecular Diagnostics, Medical University of Silesia in Katowice
   - ORCID: 0009-0009-5083-8307
3. Anna Zygmunt
   - affiliation: Department of Pathology and Molecular Diagnostics, Medical University of Silesia in Katowice
   - ORCID: 0009-0002-5849-6347
4. Wojciech Grabowski
   - affiliation: Municipal Hospital in Zabrze
   - ORCID: 0009-0006-9238-1411
5. Emilia Pedrycz
   - affiliation: Wojewódzki Szpital Zespolony w Kielcach
   - ORCID: 0009-0006-2751-2227

6. Grzegorz Drapała
   - affiliation: Wojewódzki Szpital Zespolony w Kielcach
   - ORCID: 0009-0008-1492-1544
7. Daria Pedrycz
   - affiliation: Department of Family Medicine, Medical University of Białystok
   - ORCID: 0009-0001-4988-5992

Key Words: Lavender Aromatherapy, Stress Management, Mental Health, Non-Pharmacological Interventions, Anxiety and Depression Relief

Abstract

In today's fast-paced society, rising stress levels necessitate effective management strategies. While pharmacological treatments are common, their side effects have spurred interest in alternative therapies, particularly those rooted in natural remedies. Lavender (Lavandula angustifolia), long esteemed for its calming properties, has emerged as a promising non-pharmacological option. Historical use in herbal medicine for anxiety and stress-related disorders has inspired modern scientific research to explore its potential. This review synthesizes recent studies on lavender essential oil, examining its mechanisms—such as neurotransmitter modulation—and its effectiveness in diverse settings, from reducing stress among healthcare professionals to improving sleep quality. Despite promising results, limitations like small sample sizes and variability in application methods highlight the need for more rigorous research to establish lavender's efficacy and optimize its therapeutic use in stress management and mental health care.

Introduction

In the context of escalating stress levels in contemporary society, the pursuit of effective stress management strategies has become a priority. Traditional pharmacological treatments, while efficacious for some, often carry the risk of side effects that may negate their benefits.

This paradox has catalyzed a shift towards exploring alternative and complementary therapies, with a renewed focus on the holistic properties of natural remedies. Among the myriads of botanicals employed for their therapeutic potential, lavender (Lavandula angustifolia) emerges as a particularly promising candidate, renowned for its calming and restorative effects on the human psyche and body.

Historically, lavender's sedative and anxiolytic properties have been lauded in herbal medicine, forming the backbone of its use in alleviating symptoms of anxiety, depression, and stress-related disorders. This enduring legacy of lavender in traditional healing practices has spurred contemporary scientific inquiry, seeking to validate and elucidate the mechanisms underpinning its therapeutic effects. Recent research endeavors have embarked on this quest, investigating lavender's pharmacodynamic interactions with the central nervous system and its capacity to modulate key neurochemical pathways involved in stress response (1).

The significance of these scientific explorations cannot be understated, as they offer a glimpse into the potential of lavender essential oil as a natural, non-pharmacological intervention for stress alleviation. Studies have systematically examined its efficacy in diverse settings, from enhancing mental health outcomes in older adults (2) to mitigating job-related stress among healthcare professionals (3). This body of work delineates a multi-faceted picture of lavender's anxiolytic action, endorsing its role in reducing psychological distress and enhancing wellbeing.

This review aims to synthesize findings from a spectrum of recent research on the impact of lavender essential oil on stress and related mental states. By integrating insights from clinical trials, systematic reviews, and meta-analyses, we endeavor to present a comprehensive overview of lavender's applicability and effectiveness as a complementary therapy in stress management. Drawing on evidence from key studies, we will dissect the therapeutic potential, applications, and limitations of lavender essential oil, providing a balanced evaluation of its role in contemporary stress relief paradigms.

Mechanism of Lavender Essential Oil

Lavender essential oil has garnered considerable interest for its potential benefits in managing stress and improving mental health. Research into its mechanisms of action reveals several key pharmacological effects. According to López et al. (2017), lavender essential oil modulates the NMDA receptor and serotonin transporter (SERT), which underpins its anxiolytic and antidepressant-like properties. This modulation suggests that lavender may

influence neurotransmitter systems involved in stress and mood regulation, providing a scientific basis for its therapeutic effects (1). Additionally, Ebrahimi et al. (2021) demonstrated that inhalation aromatherapy with lavender, combined with chamomile, significantly improved levels of depression, anxiety, and stress among older adults. This highlights lavender's role in promoting mental well-being through its calming effects (2). Ghavami et al. (2022) further supported lavender's efficacy, showing its effectiveness in reducing stress across various populations through a systematic review and meta-analysis (4). The physiological impact of lavender is also notable; Çiçek et al. (2022) observed reductions in stress markers such as blood pressure, heart rate, and serum cortisol in hypertensive patients using lavender oil, indicating its potential to manage stress-related physiological responses (5). While Shammas et al. (2021) reported limited statistical significance in lavender's efficacy for conditions like depression and pain in specific contexts, this underscores the need for continued research to refine its application and understand its variable effects (6). Collectively, these findings illustrate lavender's multifaceted mechanism of action, from neurotransmitter modulation to physiological stress reduction, although variability in efficacy suggests a need for further investigation to optimize its therapeutic use.

Research results

The evidence from recent studies underscores lavender essential oil's diverse and significant impact on mental health and stress management. Ebrahimi et al. (2021) demonstrated that inhalation aromatherapy with lavender and chamomile notably improved depression, anxiety, and stress levels among older adults, affirming lavender's efficacy in enhancing emotional well-being (2). Similarly, Ghavami et al. (2022) conducted a systematic review and meta-analysis that validated lavender's effectiveness in reducing stress across various populations, further establishing its role as a valuable tool in stress management (4). Çiçek et al. (2022) showed that lavender oil effectively decreased physiological markers of stress, such as blood pressure and heart rate, indicating its potential for managing both psychological and physiological aspects of stress (5). Karadağ et al. (2015) also observed significant improvements in sleep quality and reductions in anxiety among patients using lavender aromatherapy, reinforcing its utility in addressing sleep disturbances and mood disorders (7). In specialized contexts, Kianpour et al. (2016) highlighted lavender's positive impact on postpartum mental health, while Qadeer et al. (2018) found that lavender outperformed

ibuprofen in mitigating stress-induced psychological disorders, supporting its use in both general and specific therapeutic settings (8)(9).

Additionally, Sazawa et al. (2022) reported that nighttime lavender aromatherapy improved mood related to fatigue and anxiety, though without significant physiological changes, suggesting lavender's role in mood enhancement (10). Cheong et al. (2021) confirmed lavender's efficacy in improving sleep quality, demonstrating both quantitative and qualitative benefits, while Baccarani et al. (2023) found that lavender essential oil facilitated physiological recovery from cognitive stress, highlighting its role in autonomic nervous system relaxation (11)(12). Hashemi et al. (2021) also noted that blended aromatherapy, including lavender, effectively reduced test anxiety, further emphasizing its anxiety-reducing properties (13).

However, some studies provide a more nuanced view of lavender's effectiveness. López et al. (2017) and Kenda et al. (2022) explored lavender's pharmacological mechanisms and clinical applications, revealing a complex interplay of its effects and the need for additional research to fully understand its therapeutic potential (1)(14). Emadikhalaf et al. (2023) noted that while lavender was effective, its comparative benefits relative to other scents, such as rose, require further investigation to clarify its relative efficacy in stress reduction (3). Shammas et al. (2021) and Bikmoradi et al. (2015) found that lavender's benefits were limited or specific to certain conditions, suggesting variability in its effectiveness (6)(15). Aboutaleb et al. (2019) and Sebastian and Kear (2022) provided indirect support for lavender's stress management capabilities, highlighting its antioxidant properties and effects on negative affect, but indicating that more targeted studies are needed to establish clearer evidence of its efficacy (16)(17).

Furthermore, lavender's effectiveness in reducing stress, anxiety, and depression across various contexts has been extensively documented. For example, the study by Effati-Daryani et al. showed that the use of lavender cream, with or without foot baths, led to significant reductions in stress, anxiety, and depression among pregnant women, underscoring its potential as a therapeutic intervention during pregnancy (18). In high-stress work environments, such as healthcare settings, Amanak et al. found that lavender inhalation markedly decreased work-related stress and improved job satisfaction, demonstrating its efficacy in alleviating occupational stress (19). Additionally, Qadeer et al.'s research on

experimental models revealed that lavender was more effective than ibuprofen in mitigating stress-induced disorders, suggesting its broader therapeutic potential beyond conventional medicine (9). The immediate benefits of lavender were further highlighted in Wu et al.'s study, where lavender aromatherapy massage provided quick relief from work stress and burnout among female university employees, showcasing its value in acute stress management (20).

Lavender's impact extends to improving sleep quality, as evidenced by Her and Cho's systematic review and meta-analysis, which reported significant enhancements in sleep among both adults and the elderly, reinforcing lavender's utility in promoting better sleep across different age groups (21). On a neuropharmacological level, research by Masuo et al. has illustrated how lavender's aroma interacts with the brain's olfactory system to suppress stress responses, contributing to emotional regulation and overall mental well-being (22). Moreover, its relevance during global health crises, as highlighted by Shahrajabian, emphasizes lavender's broad applicability in managing elevated stress, anger, and anxiety during pandemics (23). Finally, the study by Kim et al. demonstrated that lavender oil aromatherapy not only reduces stress and bispectral index values but also alleviates pain during needle insertion, underscoring the multifaceted health benefits of lavender in clinical settings (24).

Limitations

Current research on lavender's effects on mental health and stress faces several key limitations that impact the reliability and generalizability of the findings. Methodological limitations are prominent, with many studies involving small sample sizes and short intervention durations that limit the applicability of the results beyond specific populations, such as nursing students or hospital patients (13)(20). Additionally, the lack of standardization in lavender administration—whether inhaled, applied topically, or used in varying dosages—complicates the comparison of results and the determination of optimal therapeutic methods (1)(11).

Variability in outcome measures further complicates the assessment of lavender's efficacy. Different studies use diverse psychological and physiological parameters to measure stress, anxiety, and depression, leading to inconsistencies in how outcomes are defined and evaluated

(2)(21). Moreover, the potential influence of the placebo effect or participant expectations may skew objective assessments of lavender's benefits (6)(20).

Concerns regarding long-term effects and safety are also significant. Research into the prolonged use of lavender is limited, raising questions about its sustainability and potential long-term effects (9). While generally considered safe, the potential for adverse reactions or interactions with other medications is not extensively studied, highlighting the need for more thorough investigations into lavender's safety profiles (14).

Finally, the demographic and clinical scope of existing studies is often restricted, focusing on specific groups such as pregnant women or surgical patients. This narrow focus may not accurately reflect the broader applicability of lavender aromatherapy across different populations and clinical conditions (3)(18). Addressing these limitations through more rigorous and standardized research will be crucial for fully understanding lavender's therapeutic potential and ensuring its effective use in stress management.

Practical use

Lavender has demonstrated practical utility across various settings, showcasing its versatility in supporting mental health and overall well-being. In the realm of mental health interventions, studies such as Kianpour et al. (2016) illustrate lavender's effectiveness in alleviating stress, anxiety, and depression, making it a valuable non-pharmacological option alongside traditional treatments (8). Similarly, the anti-inflammatory and analgesic properties of lavender, highlighted in research by Aboutaleb et al. (2019), suggest its suitability for post-surgical care, particularly for kidney transplant patients, where it can help manage stress and pain (16).

In academic settings, Hashemi et al. (2021) found that lavender can effectively reduce test anxiety among nursing students, indicating its potential to enhance student well-being and performance (13). Additionally, the workplace can benefit from lavender's stress-relieving qualities, as demonstrated by Amanak et al. (2023), who reported that lavender oil inhalation decreases work stress and improves job satisfaction, suggesting its role in workplace wellness programs (19).

Looking ahead, several recommendations for future research could further elucidate lavender's applications and benefits. Longitudinal studies are needed to explore the long-term effects and sustainability of lavender's benefits on mental health, as suggested by the review of nighttime lavender aromatherapy by Sazawa et al. (2022) (10). Mechanistic insights into lavender's neuropharmacology, as discussed by Masuo et al. (2021), could reveal the biochemical pathways through which lavender exerts its effects (22). Standardization of aromatherapy practices, given the variance in application methods and concentrations across studies (e.g., Wu et al. (2020)) (20), is essential for consistency and comparability of results. Expanding research to diverse populations and settings (Her & Cho, 2021) can enhance our understanding of lavender's effectiveness across different socio-cultural contexts (21). Finally, comparative studies assessing lavender against other relaxation techniques, as suggested by Bikmoradi et al. (2015), could provide a broader context for its effectiveness (15). Integrating these insights and focusing on these research areas can significantly advance the application of lavender in enhancing mental health and well-being.

Conclusion

In summary, lavender (Lavandula angustifolia) has demonstrated considerable potential as a non-pharmacological intervention for stress management and mental health enhancement. The growing body of evidence underscores its efficacy across diverse populations and contexts, from reducing anxiety and depression in pregnant women to alleviating work-related stress among healthcare professionals. Mechanistically, lavender's ability to modulate key neurotransmitter systems, as well as its impact on physiological stress markers, provides a strong foundation for its therapeutic use.

However, the research also highlights significant limitations, including small sample sizes, variability in administration methods, and a lack of long-term safety data. These limitations underscore the need for more rigorous and standardized research to fully establish lavender's effectiveness and optimize its application in clinical and everyday settings.

Practically, lavender has shown versatility, proving beneficial in settings ranging from academic environments to post-surgical care. Its integration into wellness programs, particularly in high-stress professions, offers a promising avenue for enhancing mental well-being. Future research should focus on long-term effects, standardization of treatment protocols, and comparative studies with other stress-relief methods to further validate

lavender's role as a complementary therapy in mental health care. By addressing these areas, lavender could become a more widely accepted and scientifically validated option for managing stress and improving overall mental health.

Disclosure

Author's contribution: Karolina Karoń, Łukasz Karoń, Anna Zygmunt, Wojciech Grabowski, Emilia Pedrycz, Grzegorz Drapała, Daria Pedrycz
Conceptualisation: Karolina Karoń, Łukasz Karoń, Emilia Pedrycz
Methodology: Łukasz Karoń, Karolina Karoń, Anna Zygmunt
Software: Wojciech Grabowski, Anna Zygmunt, Grzegorz Drapała
Check: Wojciech Grabowski, Karolina Karoń, Anna Zygmunt
Formal: Wojciech Grabowski, Łukasz Karoń, Anna Zygmunt
Investigation: Anna Zygmunt, Karolina Karoń, Anna Zygmunt, Daria Pedrycz
Resources: Karolina Karoń, Anna Zygmunt, Emilia Pedrycz, Grzegorz Drapała
Data curation: Łukasz Karoń, Karolina Karoń, Anna Zygmunt, Wojciech Grabowski
Writing-Rough Preparation: Karolina Karoń
Writing Review and Editing: Karolina Karoń
Visualisation: Wojciech Grabowski, Karolina Karoń, Emilia Pedrycz
Supervision: Łukasz Karoń, Wojciech Grabowski, Daria Pedrycz
Project Administration: Wojciech Grabowski, Karolina Karoń, Anna Zygmunt

All authors have read and agreed with the published version of the manuscript.

Funding statement: The study did not receive special funding.
Institutional review board statement: Not applicable.
Informed consent statement: Not applicable.
Data availability statement: Not applicable.
Conflict of interest: The authors declare no conflict of interest.

References

1. López, V., Nielsen, B., Solas, M., Ramírez, M. J., & Jäger, A. K. (2017). Exploring Pharmacological Mechanisms of Lavender (Lavandula angustifolia) Essential Oil on Central

Nervous System Targets. *Frontiers in Pharmacology*, *8*. https://doi.org/10.3389/fphar.2017.00280

2. Ebrahimi, H., Mardani, A., Basirinezhad, M. H., Hamidzadeh, A., & Eskandari, F. (2022). The effects of Lavender and Chamomile essential oil inhalation aromatherapy on depression, anxiety and stress in older community-dwelling people: A randomized controlled trial. *EXPLORE*, *18*(3), 272–278. https://doi.org/10.1016/j.explore.2020.12.012
3. Emadikhalaf, M., Ghods, A. A., Sotodeh-Asl, N., Mirmohamadkhani, M., & Vaismoradi, M. (2023). Effects of rose and lavender scents on nurses' job stress: A randomized controlled trial. *EXPLORE*, *19*(3), 371–375. https://doi.org/10.1016/j.explore.2023.01.002
4. Ghavami, T., Kazeminia, M., & Rajati, F. (2022). The effect of lavender on stress in individuals: A systematic review and meta-analysis. *Complementary Therapies in Medicine*, *68*, 102832. https://doi.org/10.1016/j.ctim.2022.102832
5. Çiçek, S. C., Demir, Ş., Yılmaz, D., Açıkgöz, A., Yıldız, S., & Yis, Ö. M. (2022). The effect of aromatherapy on blood pressure and stress responses by inhalation and foot massage in patients with essential hypertension. *Holistic Nursing Practice*, *36*(4), 209–222. https://doi.org/10.1097/hnp.0000000000000526
6. Shammas, R. L., Marks, C. E., Broadwater, G., Le, E., Glener, A. D., Sergesketter, A. R., Cason, R. W., Rezak, K. M., Phillips, B. T., & Hollenbeck, S. T. (2021). The Effect of Lavender Oil on Perioperative Pain, Anxiety, Depression, and Sleep after Microvascular Breast Reconstruction: A Prospective, Single-Blinded, Randomized, Controlled Trial. *Journal of Reconstructive Microsurgery*, *37*(06), 530–540. https://doi.org/10.1055/s-0041-1724465
7. Karadag, E., Samancioglu, S., Ozden, D., & Bakir, E. (2015). Effects of aromatherapy on sleep quality and anxiety of patients. *Nursing in Critical Care*, *22*(2), 105–112. https://doi.org/10.1111/nicc.12198
8. Kianpour, M., Mansouri, A., Mehrabi, T., & Asghari, G. (2016). Effect of lavender scent inhalation on prevention of stress, anxiety and depression in the postpartum period. *Iranian Journal of Nursing and Midwifery Research*, *21*(2), 197. https://doi.org/10.4103/1735-9066.178248
9. Qadeer, Sara et al. "Role of ibuprofen and lavender oil to alter the stress induced psychological disorders: A comparative study." *Pakistan journal of pharmaceutical sciences* vol. 31,4(Supplementary) (2018): 1603-1608.
10. Sazawa, K., Kawada, S., & Ogawa, Y. (2022). Effects of nighttime lavender aromatherapy on mood and physiological indices of stress in healthy young females. *Journal of Physical Therapy Science*, *34*(7), 503–508. https://doi.org/10.1589/jpts.34.503
11. Cheong, M. J., Kim, S., Kim, J. S., Lee, H., Lyu, Y., Lee, Y. R., Jeon, B., & Kang, H. W. (2021). A systematic literature review and meta-analysis of the clinical effects of aroma

inhalation therapy on sleep problems. *Medicine*, *100*(9), e24652. https://doi.org/10.1097/md.0000000000024652

12. Baccarani, A., Donnadieu, S., Pellissier, S., & Brochard, R. (2023). Relaxing effects of music and odors on physiological recovery after cognitive stress and unexpected absence of multisensory benefit. *Psychophysiology*, *60*(7). https://doi.org/10.1111/psyp.14251
13. Faghih, A., Hashemi, N., Nazari, F., & Forughi, M. (2021). Effects of blended aromatherapy using lavender and damask rose oils on the test anxiety of nursing students. *Journal of Education and Health Promotion*, *10*(1), 349. https://doi.org/10.4103/jehp.jehp_88_21
14. Kenda, M., Glavač, N. K., Nagy, M., & Dolenc, M. S. (2022). Medicinal plants used for anxiety, depression, or stress treatment: An update. *Molecules*, *27*(18), 6021. https://doi.org/10.3390/molecules27186021
15. Bikmoradi, A., Seifi, Z., Poorolajal, J., Araghchian, M., Safiaryan, R., & Oshvandi, K. (2015). Effect of inhalation aromatherapy with lavender essential oil on stress and vital signs in patients undergoing coronary artery bypass surgery: A single-blinded randomized clinical trial. *Complementary Therapies in Medicine*, *23*(3), 331–338. https://doi.org/10.1016/j.ctim.2014.12.001
16. Aboutaleb, N., Jamali, H., Abolhasani, M., & Toroudi, H. P. (2019). Lavender oil (Lavandula angustifolia) attenuates renal ischemia/reperfusion injury in rats through suppression of inflammation, oxidative stress and apoptosis. *Biomedicine & Pharmacotherapy*, *110*, 9–19. https://doi.org/10.1016/j.biopha.2018.11.045
17. Sebastian, L. A., & Kear, T. (2024c). The effect of lavender aromatherapy on heart rate, blood pressure, and perceived stress among cardiac rehabilitation patients. *Holistic Nursing Practice*, *38*(4), 238–244. https://doi.org/10.1097/hnp.0000000000000430
18. Effati-Daryani, F., Mohammad-Alizadeh-Charandabi, S., Mirghafourvand, M., Taghizadeh, M., & Mohammadi, A. (2015). Effect of Lavender Cream with or without Foot-bath on Anxiety, Stress and Depression in Pregnancy: a Randomized Placebo-Controlled Trial. *PubMed*, *4*(1), 63–73. https://doi.org/10.5681/jcs.2015.007
19. Amanak, K., Keleş, M. G., & Altınkaya, S. Ö. (2023). Effects of aromatherapy through inhalation on work stress and job satisfaction among health professionals. *Holistic Nursing Practice*. https://doi.org/10.1097/hnp.0000000000000586
20. Wu, C., Lee, H., Chang, C. W., Chiang, H., Tsai, Y., & Liu, H. (2020). The Immediate Effects of Lavender Aromatherapy Massage versus Massage in Work Stress, Burnout, and HRV Parameters: A Randomized Controlled Trial. *Evidence-based Complementary and Alternative Medicine*, *2020*, 1–10. https://doi.org/10.1155/2020/8830083

21. Her, J., & Cho, M. (2021). Effect of aromatherapy on sleep quality of adults and elderly people: A systematic literature review and meta-analysis. *Complementary Therapies in Medicine*, *60*, 102739. https://doi.org/10.1016/j.ctim.2021.102739
22. Masuo, Y., Satou, T., Takemoto, H., & Koike, K. (2021). Smell and Stress Response in the Brain: Review of the Connection between Chemistry and Neuropharmacology. *Molecules*, *26*(9), 2571. https://doi.org/10.3390/molecules26092571
23. Shahrajabian, M. H. (2022). Powerful stress relieving medicinal plants for anger, anxiety, depression, and stress during global pandemic. *Recent Patents on Biotechnology*, *16*(4), 284–310. https://doi.org/10.2174/1872208316666220321102216
24. Kim, S., Kim, H., Yeo, J., Hong, S., Lee, J., & Jeon, Y. (2011). The effect of lavender oil on stress, bispectral index values, and needle insertion pain in volunteers. *The Journal of Alternative and Complementary Medicine*, *17*(9), 823–826. https://doi.org/10.1089/acm.2010.0644