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Repositioning Traditional Medicine in the Modern Era: Review of Recent Publications by a Multidisciplinary Research Group from Bangladesh

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ABSTRACT

Bangladesh has a rich heritage of herbal medical practice, but unfortunately, it has been lost over time. Unlike in China, such medicines are rarely included in our modern medical practice here in Bangladesh. As the country glides along the development pathway, wide availability of better-than-before healthcare facilities is stretching our already overburdened health infrastructure to its limits. Not only are we seeing more and more patients being diagnosed with a wide array of diseases, but their expectations, need for improved care, better and cheaper medicines, etc., are all on the rise. We have been working for several years to reposition our traditional medicine and gradually integrate these into our daily practice. Here we summarize our achievements to date and also share our vision for the future.

Keywords: *Traditional medicine, modern medical practice, HCC.*

INTRODUCTION

Bangladesh is a welfare state where the constitution guarantees the right to life as a fundamental right for all its citizens as per Articles 27 to 46 of the constitution of Bangladesh [1]. This means that all Bangladeshi citizens are assured of healthcare by their government. The country has experienced huge expansion in its healthcare system and pharmaceutical sector over the last 54 years of its existence. However, it has to go a very long way to ensure this basic right to 171.5 million Bangladesh citizens. We still trail behind the World Health Organization (WHO) recommended population-to-physician ratio. Presently, we have 5 doctors, nurses, and midwives per 10,000 population [2].

Our pharmaceutical industry is a major pride for Bangladesh, which produces more than 90% of all medications needed by the country and is also a major foreign currency earner for the nation. Having said so, this is largely due to patent protection that the local pharmaceutical industry enjoys till 2033, Bangladesh being a least developed country (LDC) [3]. This means that our industry can produce any medicine without prior permission from the patent holder. However, this scenario will change drastically after 2033, when our patent protection will be non-existent and our graduation to a developing country will be complete.

Since we are non-self-sufficient in producing active pharmaceutical ingredients (API), prices of medicines are likely to soar in the country in the not-so-distant future. One option to overcome this situation, among several others, is to focus on drug discovery, which is a very expensive ball game, well beyond the means of this resource-constrained nation, not to mention we also have acute scarcity of qualified manpower to indulge ourselves in this race. For example, the US government invested at least USD 31.9 billion to develop, produce, and purchase mRNA COVID-19 vaccines [4], and Gilead Sciences, a leading pharmaceutical, spent approximately. USD 5.9 billion on research and development in 2024 only [5]. Besides, drug discovery is also time-consuming, while we have only a few years in hand.

We have a long history of traditional medicines in Bangladesh. Unfortunately, with modernization and industrialization, we have almost lost this tradition. Scientific literature in this field is almost non-existent, and the tradition mostly lives in folk practice. Besides, with the traditional wisdom being lost, this type of medical practice is largely dominated by non-qualified practitioners, thus in many cases causing harm than benefit to patients. Therefore, it is no wonder there has been no effort to integrate traditional medicines with modern medical practice in Bangladesh, which has been very well accomplished by the Chinese.

Keeping these in mind, we decided to explore whether we could prove the safety and efficacy of at least a handful of our traditional medicines, especially for the management of liver diseases, to get the ball rolling. We searched for appropriate literature, which was no easy task. Of the few references that we could identify, one was of much interest. The name of this book is Treatment of Poisons compiled by Pundit Sree Dinobondhu Datta Biddyabinod, who was a senior teacher of Mymensingh City Collegiate School, an eminent traditional medical practitioner of his time. First edition of the book was published in 1933. We got a copy of this now extinct medical literature from her granddaughter, who is in her eighties (Figure -1) [6]. In this review article, we present a summary of our achievements in this field to date and our roadmap for the future.

DISCUSSION

Our journey begins

As we started our journey, we decided to evaluate the effect of commercially available food supplements and traditional medicines produced in the West in our patients. Our early focus was on hepatocellular carcinoma (HCC), which is the sixth most common cancer and second most common cause of cancer deaths worldwide [7]. In Bangladesh, HCC ranks eighth among cancers but is third among the leading causes of deaths from cancers [8, 9, 10]. To start with, we selected a food supplement containing a combination among other constituents of *Camellia sinensis* (green tea) extract, *Cinnamomum verum* (cinnamon), and *Glycyrrhiza glabra* (glycyrrhizin) (Figure-2) (Oncoxin; Catalysis S.L., Madrid, Spain). Researchers have observed beneficial effects of other food supplements in patients with HCC [11, 12]. It has been shown that this food supplement inhibits proliferation of HCC cell lines by induction of cell cycle arrest, inhibiting cancer cell proliferation, differentiation, angiogenesis, invasion, and metastasis, and stimulating apoptosis [13]. We conducted two clinical trials in end-stage HCC patients, keeping in mind that in the absence of effective surveillance and monitoring, thousands of HCC patients present for the first time every year in Bangladesh with advanced disease [13].

The studies included 29 and 60 HCC patient,s respectively, divided into two groups: either receiving the standard of care (SOC) or the food supplement in addition to SOC. Both studies observed statistically significant improved short-term survival as well as significant improvement in quality of life among the HCC patients receiving the food supplement [13, 14].

Subsequently, we conducted another clinical trial also involving end-stage HCC. This time, we selected a different food supplement, which also qualifies as herbal medicine. It was rice bran, which is obtained from rice after removing its husk and edible endosperm (Figure-3). Rice bran contains ϒ-oryzanol, caffeic acid, ferulic acid, coumaric acid, tricin, phytic acid, vitamin E isoforms (α-tocopherol and ϒ-tocopherol), tocotrienols, phytosterols (β-sitosterol, capesterol and stigmasterol), carotenoids (α-carotene, β-carotene, lycopene and lutein), micronutrients (calcium, magnesium and vitamin B), and essential amino acids (histidine, tryptophan, arginine and cysteine) [15]. Rice bran is known for its chemopreventive effect. It increases apoptosis, reduces cell proliferation, and alters cancer cell-cycle [16]. We used commercially available rice bran (Biobran; Daiwa Pharmaceutical Co. Ltd., Tokyo, Japan) in our study. The study included 52 HCC patients. We observed improvement in quality of life and a non-significant survival benefit in the short term in the group treated with rice bran in addition SOC compared to half the patients who received SOC only [15]. Given small sample sizes in these 3 clinical trials, we opted to conclude that both these products may be useful in palliative care management of end-stage HCC patients.

Our next step forward

Having done some work with traditional herbal medicines developed in the developed West, our next step was to develop medicines ourselves from the herbs that are available locally. At this point, the world came to a standstill with the coronavirus disease-19 (COVID-19) pandemic [17]. The disease is caused by novel severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2), which is a member of the Coronaviridae family [18]. It has been identified that SARS-CoV-2 increased permeability of lungs alveoli and induces cytokine storm and multi-organ failure due to suppression of angiotensin converting enzyme 2 (ACE2) activity [19, 20].

We identified a native spiny herb, *Euphorbia neriifolia* (dudsor) (Figure-4), which has anti-inflammatory, anti-bacterial, and anti-parasitic properties. It is used in traditional medicine for treating human cough, bronchitis, and asthma in addition to delirium, leukoderma, hemorrhoids, and malignancies [21, 22, 23, 24, 25]. Several secondary metabolites like triterpenes, anthocyanins, and diterpenes have been isolated from *Euphorbia neriifolia.* We isolated 17 bioactive compounds from *Euphorbia neriifolia,* namely, delphin, epi-friendelanol, tulipanin, taraxerol, pelargonin, nerifoliol, lathyrane, kurane, isopimarane, euphorbol, euphorbiasteroid, euphol, cycloartenol, bata-amyrin, atisane, antiquorin and abetane it. We utilized a combination of molecular profiling, absorption, distribution, metabolism, elimination, and toxicological (ADMET) profiling and molecular dynamics simulation (MDS) studies to assess the effectiveness of these compounds against the SARS-CoV-2 target protein ACE-2 ligand binding site [26]. We found that delphin, which is an *Euphorbia neriifolia* leaf extract, had the highest affinity for SARS-CoV-2 receptor protein 6VW1. It has been shown that Delphin generates interleukin-1 (IL-1), reduces cytokine production, boosts T cell function, and interferes with SARS-Cov-2 attachment [27, 28, 29, 30].

We therefore hypothesized that delphin may be a potential inhibitor of SARS-CoV-2. We employed ADMET profiling for systemic virtual potential drug screening as an alternative to *in vivo* study. Delphin showed 3 violations of Lipinski rule, which is an important criterion for identifying the pharmacological efficacy of any molecule in humans [31].

With these results in hand, we decided to conduct a clinical trial of *Euphorbia neriifolia* in COVID-19 patients. By that time OMICRON variant of SARS-CoV-2 became dominant in the pandemic scenario, which was more infectious but less pathogenic [32]. We conducted an open-label observational, controlled study involving 60 mild to moderate COVID-19 patients divided into 4 groups. Unlike their 15 counterparts who received only SOC, the 15 moderate COVID-19 patients who received *Euphorbia neriifolia* leaf and juice in addition to SOC showed decreased C-reactive protein (CRP) and D-dimer levels and an increase in oxygen concentration within 7 days. Similarly, hospital stay was also significantly reduced in both mild and moderate COVID-19 patients receiving *Euphorbia neriifolia* plus SOC, compared to those on SOC alone. It was thus suggested that *Euphorbia neriifolia* may be beneficial in managing COVID-19, although no conclusive decision could be made due to our small sample size [33].

Widening our horizon

At this point, we also started concentrating on how to ensure the best possible outcome from the local herbs. In one of our recent studies, we focused on *Andrographis paniculata*, a medicinal herb, well known for his hepatoprotective role *Andrographis paniculata (*green chiretta) (Figure-5) [34]. Most of the therapeutic efficacy of this herb is attributed to andrographolide, which is a crystalline, bicyclic compound. In addition to it's hepatoprotective effect, andrographolide has a range of therapeutic efficacies including anti-inflammatory, anti-viral, anti-microbial, antioxidant, anti-cancer, anti-diabetic and wound healing properties [35, 36, 37, 38, 39, 40, 41]. More than 2% of andrographolide is in the leaves of *Andrographis paniculata.* It is known that andrographolide degrades if kept for long in inappropriate storage conditions; the reason why we decided to look into this issue [42]. In our study, we collected fresh samples that were immediately processed into powder form, 1-year-old samples stored in humid conditions at room temperature (25^0 to 40^0), and 99% pure pharmaceutical grade andrographolide. We extracted andrographolide using alcohol solvent and assessed its concentration using high-performance liquid chromatography (HPLC) [43]. We found the average concentration of andrographolide in fresh samples to be 234.5 µgm/mL, much higher than that in the preserved samples, which was only 87.39 µgm/mL [43]. This degradation was attributed to moisture. We therefore concluded that it is extremely important to ensure proper storage of herbs to obtain their best medicinal value.

The way forward

Based on the encouraging findings of our research with local herbs and the experience thus gathered, we searched our traditional medical literature further and identified some herbs, which we believe may have beneficial effects on a range of liver diseases like fatty liver, liver cirrhosis, and advanced-stage HCC. These include *Silybum marianum* (silymarin), *Moringa oleifera* (moringa), *Terminalia Arjuna* (arjun), *Phyllanthus emblica* (amlaki), and *Carica papaya* (papaya) (Figure-6) to name a few [6].

Over the last few years, we have conducted molecular docking, safety, and efficacy studies in animal models as well as clinical trials of these herbs in humans. Our results are encouraging, and we are in the process of publishing in the coming days.

CONCLUSION

As the burden of communicable diseases is on the rise both globally and at home, and with increased awareness and easier access to advanced diagnostic modalities, more and more patients are being diagnosed with liver diseases in Bangladesh, as elsewhere in the globe. The quest for newer and better drugs to manage such conditions will be ever-increasing. Given that drug discovery is a multi-million-dollar effort, well beyond the reach of researchers like us from resource-constrained countries like Bangladesh, we hypothesized that we may be able to identify useful remedies from our rich, but lost, heritage of herbal medicines. We are optimistic that our efforts will encourage more medical scientists from Bangladesh as well as our region to undertake similar research in different branches of medical science, thus paving the way for repositioning our traditional herbal medicines in our modern-day prescriptions, both to the benefit of our patients and our healthcare system.

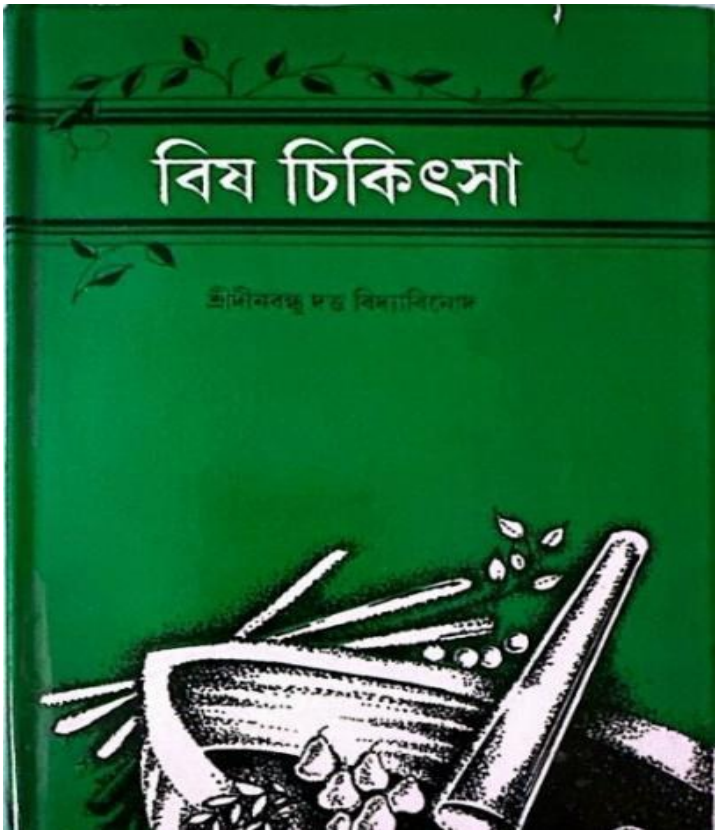

Figure-1: Cover book titled Treatment of Poisons

Figure-2: Camellia sinensis (Green tea), Cinnamomum verum (cinnamone), Glycyrrhiza glabra (glycyrrhizin)

Figure-3: Paddy

Figure-4: Euphorbia neriifolia (dudsor)

Figure-5: Andrographis paniculata (green chiretta)

Figure-6: Silybum marianum (silymarin), Moringa oleifera (moringa), Terminalia Arjuna (arjun), Phyllanthus emblica (amlaki), Carica papaya (papaya)

REFERENCES

1. http://bdlaws.minlaw.gov.bd/act-367.html

2. https://www.who.int/bangladesh/news/detail/06-04-2021-from-unqualified-to-professional-medicine-bangladesh-a-promising-journey

3. Chaudhuri S. Product Patent Protection, the TRIPS LDC Exemption and the Bangladesh Pharmaceutical Industry. ResearchGate September 2021.

4. Lalani HS, Nagar S, Sarpatwari A, Barenie RE, Avorn J, Rome BN, Kesselheim AS. US public investment in development of mRNA covid-19 vaccines: retrospective cohort study. BMJ. 2023 Mar 1;380:e073747. doi: 10.1136/bmj-2022-073747. Erratum in: BMJ. 2023 Mar 14;380:p587. doi: 10.1136/bmj.p587. PMID: 36858453; PMCID: PMC9975718.

5. https://www.statista.com/statistics/274510/spending-on-research-and-development-by-gileadsciences/#:~:text=Gilead%20Sciences'%20spending%20on%20research%20and%20development%202008%2D2024&text=Gilead%20Sciences%20spent%20some%205.9,development%20from%202008%20to%202024.

6. Biddyabinod DBD. Treatment of Poisons (Bish Chikitsha). Second edition; published 1998.

7. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136(5):p. 359–386. DOI: 10.1002/ ijc.29210.

8. Jabeen S, Islam MJ, Talukder MH, et al. Pathoepidemiology of Cervical Cancer in National Institute of Cancer Research and Hospital of Bangladesh. Journal of Dhaka Medical College 2015;23(2):p.203–210. DOI: 10.3329/jdmc.v23i2.25392.

9. Mahtab MA, Karim F, Foster G, et al. Prevalence and risk factors of asymptomatic hepatitis C virus infection in Bangladesh. J Clin Exp Hepatol 2011;1(1):p.13–16. DOI: 10.1016/S0973-6883(11)60111-4. PMID: 25755305; PMCID: PMC3940088.

10. Hussain SA, Sullivan R. Cancer control in Bangladesh. Jpn J Clin Oncol 2013;43(12):p.1159–1169. DOI: 10.1093/jjco/hyt140. PMID: 24163419; PMCID: PMC3842101.

11. Matsui Y, Uhara J, Satoi S, Kaibori M, Yamada H, Kitade H, *et al*. Improved prognosis of postoperative hepatocellular carcinoma patients when treated with functional foods: A prospective cohort study. J Hepatol 2002;37:78-86.

12. Morihara D, Iwata K, Hanano T, Kunimoto H, Kuno S, Fukunaga A, et al. Late-evening snack with branched-chain amino acids improves liver function after radiofrequency ablation for hepatocellular carcinoma. Hepatol Res 2012;42:658-67.

13. Al-Mahtab M, Akbar SM, Khan MS, Rahman S. Increased survival of patients with end-stage hepatocellular carcinoma due to intake of ONCOXIN®, a dietary supplement. Indian J Cancer. 2015 Jul-Sep;52(3):443-6. doi: 10.4103/0019-509X.176699. PMID: 26905163.

14. Mahtab MAI, Ahmed F, Das DC, *et al*. Effect of Oncoxin, a Food Supplement, on Terminal-stage Hepatocellular Carcinoma Patients. Bengal Physician Journal 2021;8(3):63–66.

15. Ashrafujjaman M, Mahtab MA, Noor-E-Alam SM, Rahim MA, Das DC, Ahmed F, Mamun AA, Mahmud T, Mahmood T. Role of Biobran (Arabinoxylan Rice Bran) on Patients with Advanced Stage Hepatocellular Carcinoma. Euroasian J Hepatogastroenterol. 2023 Jul-Dec;13(2):84-88. doi: 10.5005/jp-journals-10018-1407. PMID: 38222955; PMCID: PMC10785141.

16. Henderson AJ, Ollila CA, Kumar A, et al. Chemopreventive properties of dietary rice bran: Current status and future prospects. Adv Nutr 2012;3(5):643–653. DOI: 10.3945/an.112.002303.

17. Zhang T, Wu Q, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. Curr Biol 2020;30(7):1346– 1351.e2. DOI: 10.1016/j.cub.2020.03.022.

18. Ciotti M, Angeletti S, Minieri M, et al. COVID-19 outbreak: An overview. Chemotherapy 2019;64(5–6):215–223. DOI: 10.1159/000507423.

19. Machado D, Girardini M, Viveiros M, et al. Challenging the drug-likeness dogma for new drug discovery in tuberculosis. Front Microbiol 2018;9:1367. DOI: 10.3389/fmicb.2018.01367.

20. Li G, De Clercq E. Therapeutic options for the 2019 novel coronavirus (2019-nCoV). Nat Rev Drug Discov 2020;19(3):149–150. DOI: 10.1038/ d41573-020-00016-0.

21. Thorat BR, Bolli V. A review on euphorbia neriifolia plant. International Research Journal of Modernization in Engineering Technology and Science 2017;1(6):1723–1732. DOI: http://dx.doi.org/10.26717/BJSTR.2017.01.000523.

22. Hohmann J, Molnár J. [Euphorbiaceae diterpenes: plant toxins or promising molecules for the therapy?]. Acta Pharm Hung 2004;74(3):149–157. PMID: 16318224.

23. Betancur-Galvis LA, Morales GE, Forero JE, et al. Cytotoxic and antiviral activities of Colombian medicinal plant extracts of the Euphorbia genus. Memórias do Instituto Oswaldo Cruz 2002;97(4):541–546. DOI: https://doi.org/10.1590/s0074-02762002000400017.

24. Gaur K, Rana AC, Nema RK, et al. Anti-inflammatory and analgesic activity of hydro-alcoholic leaves extract of Euphorbia neriifolia Linn. Asian J Pharm Clin Res 2009;2(1):26–28. Available from: https://www.researchgate.net/publication/228448383.

25. Kumara SM, Neeraj P, Santosh D, et al. Phytochemical and antimicrobial studies of leaf extract of Euphorbia neriifolia. Journal of Medicinal Plants Research 2011;5(24):5785–5788. Available from: http://www.academicjournals.org/JMPR.

26. Pramanik, Md Enayet Ali, Rukhshana Akhter Jahan, Akm Azad-Ud-Doula Prodhan, Md Royhan Gofur, Humayra Haque, Md Nur Islam, Md Ashraful Islam, et al. 2023. "Identification of Leading Compounds from Euphorbia Neriifolia (Dudsor) Extracts as a Potential Inhibitor of SARS-CoV-2 ACE2-RBDS1 Receptor Complex: An Insight from Molecular Docking ADMET Profiling and MD-Simulation Studies." Euroasian Journal of Hepato-Gastroenterology 13 (2): 89–107. https://doi.org/10.5005/jp-journals-10018-1414.

27. Ikuta K, Mizuta K, Suzutani T. Anti-influenza virus activity of two extracts of the blackcurrant (Ribes nigrum L.) from New Zealand and Poland. Fukushima J Med Sci 2013;59(1):35–38. DOI: https://doi. org/10.5387/fms.59.35.

28. Ren Z, Na L, Xu Y, et al. Dietary supplementation with lacto-wolfberry enhances the immune response and reduces pathogenesis to influenza infection in mice. J Nutr 2012;142(8):1596–1602. DOI: https:// doi.org/10.3945/jn.112.159467.

29. Calland N, Dubuisson J, Rouillé Y, et al. Hepatitis C virus and natural compounds: A new antiviral approach? Viruses 2012;4(10):2197–2217. DOI: https://doi.org/10.3390/v4102197.

30. Vázquez-Calvo Á, Jiménez de Oya N, Martín-Acebes MA, et al. Antiviral properties of the natural polyphenols delphinidin and epigallocatechin gallate against the flaviviruses West Nile virus, Zika virus, and dengue virus. Front Microbiol 2017;8:1314. DOI: https://doi.org/10.3389/fmicb.2017.01314.

31. Lipinski CA, Lombardo F, Dominy BW, et al. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced drug delivery reviews 1997;23(1–3):3–25. DOI: https://doi.org/10.1016/S0169- 409X(96)00423-1.

32. Kannan S, Shaik Syed Ali P, Sheeza A. Omicron (B.1.1.529)–variant of concern–molecular profile and epidemiology: a mini review. Eur Rev Med Pharmacol Sci 2021;25(24):8019–8022. DOI: 10.26355/ eurrev_202112_ 27653.

33. Pramanik MEA, Miah MMZ, Ahmed I, Hossain AM, Ali MN, Haque MJ, Islam AM, Jahan RA, Haque ME, Rahman MM, Islam MS, Alam MM, Basak PM, Jamil AM, Mamun SMAA, Islam MR, Rahman MM, Shafikuzzaman H, Suman MAA, Badol MMH, Rahman M, Hasan MS, Mondal MNI, Kabir MM, Rahman MM, Haque H, Mahtab MA, Akbar SMF. *Euphorbia neriifolia* Leaf Juice on Mild and Moderate COVID-19 Patients: Implications in OMICRON Era. Euroasian J Hepatogastroenterol. 2022 Jan-Jun;12(1):10-18. doi: 10.5005/jp-journals-10018-1367. PMID: 35990866; PMCID: PMC9357524.

34. Senthil Kumaran K, Thirugnanasambantham P, Viswanathan S, Sree M, Murthy R. An HPLC method for the estimation of andrographolide in rabbit serum, 2003. [Online]. Available: https://www.researchgate.net/ publication/294271003.

35. Dai Y, Chen SR, Chai L, Zhao J, Wang Y, Wang Y. Overview of pharmacological activities of Andrographis paniculata and its major compound andrographolide. Crit Rev Food Sci Nutr. 2019;59:S17-S29. doi:10.1080/10408398.2018.150 1657.

36. Pongtuluran OB, Rofaani E. Antiviral and immunostimulant activities of Andrographis paniculata. HAYATI J Biosci. 2015;22(2):67-72. doi:10.4308/hjb.22.2.67.

37. Murugan K, Selvanayaki K, Al-Sohaibani S. Antibiofilm activity of Andrographis paniculata against cystic fibrosis clinical isolate Pseudomonas aeruginosa. World J Microbiol Biotechnol. 2011;27(7):1661-1668. doi:10.1007/s11274-010-0620-3.

38. Rao PR, Rathod VK. Rapid extraction of andrographolide from Andrographis paniculata Nees by three-phase partitioning and determination of its antioxidant activity. Biocatal Agric Biotechnol. 2015;4(4):586-593. doi:10.1016/j.bcab.2015.08.016.

39. Suriyo T, Chotirat S, Rangkadilok N, Pholphana N, Satayavivad J. Interactive effects of Andrographis paniculata extracts and cancer chemotherapeutic 5-Fluorouracil on cytochrome P450s expression in human hepatocellular carcinoma HepG2 cells. J Herb Med. 2021;26:100421. doi:10.1016/j.hermed.2021.100421.

40. Imani SF, Khairani AA, Arbianti R, Utami TS, Hermansyah H. The effect of fermentation time and sonication temperatures on extraction process of bitter leaves (Andrographis paniculata) against antidiabetic activity through α-glucosidase enzyme inhibition test. AIP Conf Proc. 2020;2255. doi:10.1063/5.0015260.

41. Jamaludin R, Mohd N, Safazliana R, Sulong R, Yaakob H. Andrographis paniculata-loaded niosome for wound healing application: characterisation and in vivo analyses. J Drug Deliv Sci Technol. 2021;63:102427. doi:10.1016/j. jddst.2021.102427.

42. Plubrukarn A, Pinsuwan S, Ingkatawornwong S, Supavita T. Stability of andrographolide in powdered andrographis herb under accelerated conditions. Planta Med. 2006;72(10):954-956. doi:10.1055/s-2006-946696.

43. Ahammed MT, Sultan MZ, Hossain MS, Al Mahtab M, Bachar SC. Degradation of andrographolide in Andrographis paniculata over 1 year storage. Phytochem Anal. 2025 Jan;36(1):289-295. doi: 10.1002/pca.3441. Epub 2024 Aug 28. PMID: 39205402.