EJPMR, 2026, 13(5), 386-393 **Review Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

ADVANCEMENTS FORMULATION AND PHARMACOLOGICAL EVALUATION OF ALOE SPECIES AND HIBISCUS SABDARIFFA FOR CANCER SUPPORTIVE CARE: A COMPREHENSIVE REVIEW (2010-2025)

Abdalwali Ahmed Saif[1], Amina El-Shaibany[2,4], Mahmoud Mahyoob Alburyhi[1]*, Mohammed Abbas Hamidaddin[3], Maged Alwan Noman[1,4]

*[1]Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[2]Professor Dr. of Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[3]Asst. Prof. Dr. of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[4]Department of Pharmacy, Faculty of Medical Sciences, Al-Yemenia University, Sana'a, Yemen.

***Corresponding Author: Mahmoud Mahyoob Alburyhi**

Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

DOI: https://doi.org/10.5281/zenodo.20023036

How to cite this Article: Abdalwali Ahmed Saif[1]*, Amina El-Shaibany[2,4], Mahmoud Mahyoob Alburyhi[1]*, Mohammed Abbas Hamidaddin[3] and Maged Alwan Noman[1,4]. (2026). Advancements Formulation And Pharmacological Evaluation Of Aloe Species And Hibiscus Sabdariffa For Cancer Supportive Care: A Comprehensive Review (2010-2025). European Journal of Pharmaceutical and Medical Research, 13(5), 386–393.
This work is licensed under Creative Commons Attribution 4.0 International license.

Article Received on 05/03/2026 **Article Revised on 25/04/2026** **Article Published on 04/05/2026**

ABSTRACT

Background: Cancer supportive care relies on managing symptoms, mitigating treatment side effects, and improving patient quality of life. Herbal supplements containing antioxidant-rich and immunomodulatory botanicals are increasingly integrated into oncological care. **Objective:** To systematically review the pharmaceutical formulation development and pharmacological evaluations of *Aloe* species and *Hibiscus sabdariffa* from 2010 to 2025, establishing a scientific foundation for their use in cancer supportive care. **Methods:** A detailed literature review was conducted analyzing solid dosage formulations, microencapsulation technologies, and extraction optimizations, alongside *in vitro* and *in vivo* evaluations of anticancer, anti-inflammatory, and immunomodulatory mechanisms. **Discussion:** Advanced formulation strategies—including sustained-release matrix tablets, cross-linked hydrogels, and nanoencapsulation—have successfully overcome the physical limitations and instability of *Aloe* and *Hibiscus* extracts. Pharmacologically, *Aloe* species demonstrate profound immunomodulatory and anti-inflammatory properties, while acting as potent bioenhancers. Conversely, *Hibiscus sabdariffa* exhibits direct cytotoxic effects, inducing apoptosis via AMPK activation and generating targeted oxidative stress in cancer cells, alongside significant synergistic antitumor efficacy when combined with conventional chemotherapeutics. **Conclusion:** The integration of modern pharmaceutical formulation technologies with the potent pharmacological activities of *Aloe* and *Hibiscus* extracts yields highly stable, bioavailable, and efficacious herbal supplements. These standardized botanical therapies hold immense promise for enhancing comprehensive cancer supportive care.

KEYWORDS: Cancer Supportive Care; *Aloe vera*; *Hibiscus sabdariffa*; Pharmaceutical Formulation; Microencapsulation; Phytopharmacology.

1. INTRODUCTION

Cancer supportive care encompasses a continuum of interventions aimed at managing debilitating symptoms, reducing the severe side effects of conventional treatments, and improving the overall quality of life for oncology patients. In recent years, herbal supplements have gained substantial traction as complementary approaches. Botanicals rich in antioxidants and

immunomodulatory compounds are uniquely positioned to mitigate treatment-related toxicities. This review comprehensively examines the literature from 2010 to 2025 regarding the pharmaceutical formulation and pharmacological validation of two highly promising botanical groups: *Aloe* species and *Hibiscus sabdariffa*.

2. *Aloe* Species: Pharmaceutical Formulation and Development

2.1 Solid Dosage Forms and Matrix Tablets

Transitioning crude *Aloe* extracts into viable clinical therapies requires robust formulation techniques. Patel developed effervescent tablets incorporating *Aloe vera* extract to enhance palatability and achieve rapid dissolution. Utilizing citric acid and sodium bicarbonate alongside *Aloe vera* gel powder, the tablets disintegrated in under 3 minutes, maintained satisfactory hardness (4–6 kg/cm²), and successfully preserved *Aloe* bioactive compounds post-compression.[1] Validating oral clinical applications, Fallah Huseini et al. conducted a randomized, double-blind, placebo-controlled trial using *Aloe vera* leaf gel capsules (300 mg). Filled using a hand-operated machine, these gelatin capsules demonstrated excellent clinical safety and significantly reduced fasting blood glucose and lipid profiles in diabetic patients.[2]

Aloe vera has also been heavily utilized as an active excipient. Ranade et al. engineered bilayer floating tablets combining amoxicillin and *Aloe vera* gel powder for gastric retention. Using direct compression with HPMC K4M/K100M and effervescent agents, the formulation achieved a floating time of over 8 hours, delivering enhanced gastroprotective activity.[3] Similarly, Rahman et al. formulated sustained-release curcumin matrix tablets using *Aloe vera* mucilage (5–15% w/w) as a natural solubility enhancer. The freeze-dried *Aloe* polysaccharide fraction significantly improved curcumin dissolution (up to 78% at 8 hours) and increased bioavailability by 200%, establishing *Aloe vera* as a dual release-modifier and bioenhancer.[4]

For traditional medicine standardization, Moein et al. formulated film-coated tablets of "Alvoo Fix" (an *Aloe*-based medicine) using wet granulation with PVP K30. They established comprehensive quality control parameters, quantifying aloin content via HPLC and achieving >75% dissolution in 60 minutes.[5] Rao et al. further validated *Aloe vera* gel powder (10–30% w/w) as an effective natural matrix former for cardiovascular drug delivery, achieving optimal sustained release of eplerenone over 8–12 hours.[6]

2.2 Analytical Quality Control and Advanced Delivery Systems

To address the long-term stability of *Aloe* markers, Girreser and Wolfram developed a band-selective quantitative HSQC NMR method for *Aloe vera* and *Aloe ferox* solid dosage forms. This advanced technique enabled the simultaneous quantification of acemannan, aloin, and aloe-emodin, revealing specific degradation patterns after 12 months of storage.[7]

Exploring systemic efficacy, Na et al. demonstrated that orally administered processed *Aloe vera* gel (PAG) capsules containing low molecular weight polysaccharides retained high biological activity, successfully suppressing serum IgE and inflammatory cytokines.[8] Additionally, Ashwini et al. proved that *Aloe vera* mucilage acts as a highly effective, biocompatible natural binding agent in immediate-release tablets, achieving optimal friability and drug release profiles comparable to synthetic microcrystalline cellulose.[9] Jani et al. corroborated these release-retarding properties, formulating matrix tablets with processed *Aloe vera* gel that followed Higuchi diffusion-controlled kinetics for up to 12 hours.[10]

Recent innovations have focused on overcoming the rapid hydration limitations of native *Aloe* polysaccharides. Irfan developed a citric acid cross-linked *Aloe vera* hydrogel (CL-ALH). Chemical cross-linking at 120°C drastically reduced equilibrium swelling and achieved a precise 24-hour sustained release, maintaining >92% drug content stability for 6 months.[11] Furthermore, Tevlek et al. pioneered chitosan-encapsulated *Aloe vera* extract nanoparticles (AVE-CSNPS) prepared by ionic gelation. These nanoparticles exhibited an 86.2% encapsulation efficiency, sustained 48-hour release, and provided a 2.8-fold higher cellular uptake, representing a next-generation formulation strategy.[12]

3. *Aloe* Species: Pharmacological Evaluation

3.1 Cytotoxic and Anticancer Mechanisms

The antineoplastic potential of *Aloe* is widely documented. Al-Mahbashi et al. evaluated the cytotoxic activities of *Aloe rubroviolacea*, *Aloe vera*, and *Aloe sabaea* flower extracts against 11 human cancer cell lines. *Aloe vera* exhibited the strongest concentration-dependent growth inhibition (up to 67%), while *A. rubroviolacea* demonstrated moderate antiproliferative capacities (up to 42% inhibition).[13] Focusing on specific pathways, Tabolacci et al. proved that *Aloe vera* gel exhibits significant anti-melanoma activity. It induced

p53 tumor suppressor protein activation, upregulated the p21 cell cycle inhibitor, triggered caspase-3-mediated apoptosis, and caused G1 phase cell cycle arrest.[14]

Evaluating advanced models, Tevlek et al. assessed *Aloe vera* on 3D liver tumor spheroids, demonstrating a powerful 68% growth inhibition compared to only 42% in 2D cultures. Mechanistically, the extract induced profound mitochondrial dysfunction, increased reactive oxygen species (ROS) generation by 3.8-fold, and activated autophagy, establishing its relevance for hepatocellular carcinoma.[12]

3.2 Immunomodulatory and Anti-inflammatory Effects

Aloe species are potent immunomodulators. Liu et al. investigated an *Aloe*-based composition (UP360) in an accelerated aging mouse model. The treatment significantly improved innate and adaptive immunity, increasing NK cell cytotoxicity (2.6-fold), macrophage phagocytosis, and CD4+/CD8+ T cell counts, while preserving the thymus from aging-associated damage.[15] Memorial Sloan Kettering Cancer Center's comprehensive review corroborated this, documenting that the polysaccharide acemannan stimulates TNF-α, IL-1β, and IL-6 production in macrophages and acts as a potent immunostimulator via the NF-κB pathway.[16]

Targeting inflammation, Yagi et al. conducted molecular docking which identified Aloesin as a top-performing TNF-α inhibitor. Aloesin effectively suppressed the cyclooxygenase pathway and reduced prostaglandin and histamine release, positioning it as a promising candidate for cancer-related inflammation.[17] Li et al. provided a massive review (2020–2025) on *Aloe vera* polysaccharides, affirming that high molecular weight fractions (>400 kDa) exhibit superior immunomodulatory potency, profound COX-2/NF-κB inhibition, and highly effective DPPH radical scavenging.[18] Finally, Yanikoglu et al. proved *in vivo* that oral *Aloe vera* formulations significantly reduced allergic airway inflammation, diminished Th2 cytokines, and thinned mucosal thickness, highlighting the therapeutic role of the active component aloin.[19]

4. *Hibiscus sabdariffa*: Pharmaceutical Formulation and Development

4.1 Extraction Optimization and Stability Kinetics

Formulating *Hibiscus sabdariffa* requires managing the thermal sensitivity of its bioactive anthocyanins. A foundational study by Mourtzinos et al. evaluated the thermal stability of *H. sabdariffa* extracts. They demonstrated that β-cyclodextrin complexation decreased the degradation rate and protected anthocyanins up to 250°C, providing a massive 3.4-fold improvement in thermal stability for solid dosage forms.[20] Clinically, early formulation studies by Lin et al. successfully utilized *H. sabdariffa* extract capsules (1g) to significantly reduce serum cholesterol in hypercholesterolemic patients without adverse events.[21]

Extraction solvent selection is critical. Sindi demonstrated that aqueous and methanolic extracts yielded the highest anthocyanin content (delphinidin-3-sambubioside and cyanidin-3-sambubioside) and the strongest DPPH antioxidant activity.[22] Moving to tablet development, Herrera-Arellano et al. successfully formulated *H. sabdariffa* aqueous extract tablets using wet granulation, achieving excellent friability (<0.8%) and drug content uniformity for use as an antihypertensive adjuvant.[23]

Storage stability is heavily reliant on temperature and pH. Sinela et al. investigated anthocyanin degradation kinetics, establishing that isothermal degradation follows first-order kinetics. They calculated half-lives of 90 days at 25°C and 56 days at 40°C, proving that matrix composition and ionic strength are vital for optimizing supplement storage.[24]

4.2 Microencapsulation and Spray-Drying Technologies

To protect thermolabile compounds, modern formulation relies heavily on microencapsulation. Ridzwan et al. developed spray-dried powders of *H. sabdariffa* ethanolic extracts. Optimized spray drying (inlet 80°C) produced powders with excellent flow properties suitable for direct compression while preserving potent α-amylase inhibitory activities and high phenolic content.[25] Nguyen et al. expanded on this by microencapsulating anthocyanins with a maltodextrin carrier at high temperatures (160°C). The optimal formulation yielded >85% encapsulation efficiency and >93% solubility, effectively protecting the anthocyanins from environmental degradation.[26]

Ariestanti et al. successfully explored *H. sabdariffa* calyx extracts as natural colorants and active ingredients, establishing formulation standardizations based on precise anthocyanin content matching for semi-solid and solid dosage forms.[27] To optimize initial yields, Yagi et al. determined that infusion and decoction extraction methods yielded 1.5 to 2.1-fold higher total phenolic and anthocyanin contents compared to standard

maceration.[28] Idham et al. confirmed that spray-drying microencapsulation using a maltodextrin and whey protein isolate matrix (1:3 core: wall ratio) resulted in exceptional post-processing retention (82.6%) and dramatically extended the anthocyanin half-life during high-humidity storage.[29]

5. *Hibiscus sabdariffa*: Pharmacological Evaluation

5.1 Antioxidant and Metabolic Regulation

The pharmacological efficacy of *H. sabdariffa* is driven by its dense phenolic profile. Banwo et al. demonstrated that ethyl acetate fractions of the calyces exhibit extreme antioxidant activity (98% ABTS inhibition) alongside powerful α-amylase and α-glucosidase inhibitory actions. This establishes *Hibiscus* as an excellent functional ingredient for targeting oxidative stress and hyperglycemia.[30] Suhartika et al. evaluated its effects on insulin resistance using network pharmacology, showing that *Hibiscus* downregulates HIF-1α expression in diabetic models, subsequently lowering cholesterol, triglycerides, and lipid peroxidation while significantly boosting catalase and glutathione activity.[33]

5.2 Anticancer Mechanisms and Apoptosis

Hibiscus extracts possess profound, selective anticancer mechanisms. Chiu et al. elucidated that *Hibiscus* extract selectively induces pro-oxidant effects specifically in MCF-7 breast cancer cells. It altered the intracellular redox status by deeply depleting antioxidant enzymes (SOD, catalase, glutathione peroxidase) and increasing MDA lipid peroxidation 4.2-fold, triggering oxidative stress-mediated apoptosis while protecting normal, healthy cells.[31]

Tsai et al. investigated the specific apoptotic signaling pathways of *Hibiscus* anthocyanins in colorectal cancer cells. The extracts heavily activated AMPK signaling (2.8-fold increase), inhibited the Akt survival pathway, induced mitochondrial dysfunction (cytochrome c release), and triggered Fas-mediated extrinsic apoptosis via caspase-8 and caspase-3 activation. *In vivo* dietary supplementation in mice remarkably reduced polyp numbers by 54% and size by 67%.[32] A comprehensive review by Ahmed et al. synthesized this evidence, confirming that *Hibiscus* induces apoptosis, triggers G1 and G2/M phase cell cycle arrest, inhibits VEGF-mediated angiogenesis, and prevents metastasis via MMP-2/9 downregulation across oral, breast, lung, colon, and leukemia cell lines.[34]

5.3 Synergistic and Immunotherapeutic Potential

The combination of *Hibiscus* with conventional therapies highlights its supportive care value. Ezcurra-Hualde et al. demonstrated that intratumoral administration of *H. sabdariffa*-derived anthocyanins produced massive tumor mass reductions. Crucially, combination with doxorubicin achieved highly synergistic effects (88.2% tumor growth inhibition). Mechanistically, the extract reversed chemotherapy-induced immunosuppression, enhanced CD8+ T cell tumor infiltration, increased NK cell activity, and induced long-term immune memory.[35] Lastly, Nogueira da Cruz comprehensively reviewed its selective cytotoxicity, documenting that *Hibiscus* specifically targets ERα-positive breast cancer cells. It heavily downregulates ERα expression, triggers apoptosis via Bax/Bcl-2 modulation, suppresses NF-κB nuclear translocation, and inhibits COX-2, proving its immense, multifaceted value in hormone-dependent cancers.[36]

Preformulation study is a stage before preparing drugs is the stage of compatibility between excipients and the drug, and after that the various pharmaceutical forms are prepared according to compatibility. the method of preparing drugs from industrial sources applies to natural sources, taking into account that natural sources need to be studied from the beginning, as there is no information available. Therefore, the study must be in accordance with the system of studying compatibility preformulation, then studying the formulation, evaluation, and stability study of pharmaceutical forms in novel drug delivery systems. Formulating natural sources and herbal extracts as advanced drug delivery systems that have been developed and formulated in different pharmaceutical dosage forms and therapeutic doses appropriate to the type of diseases such as acute, chronic, or emergency cases and the principles and strategies of treating them, whether direct, auxiliary, or preventive treatment. They are distinguished by their safe and effective natural drug use according to scientific studies determined by pharmacognosy and pharmaceutical formulation Scientists.[37-68]

6. CONCLUSION

The rigorous pharmaceutical and pharmacological evaluation of *Aloe* species and *Hibiscus sabdariffa* from 2010 to 2025 firmly establishes their vital role in cancer supportive care. Pharmaceutical advancements—ranging from targeted microencapsulation and citric acid cross-linked hydrogels to optimized effervescent and sustained-release matrix tablets—have successfully mitigated the physical instability and poor solubility of

these crude extracts. Pharmacologically, these botanical formulations offer immense therapeutic value; *Aloe* provides critical immune modulation and hepatoprotective antioxidant defenses, while *Hibiscus sabdariffa* delivers targeted cytotoxic, pro-apoptotic, and synergistic anti-tumor effects. Together, standardized formulations of these plants offer a scientifically validated, reproducible, and highly effective complementary approach to mitigating treatment toxicities and improving oncology patient outcomes.

REFERENCES

1. Patel, Salim & Siddaiah, M. Formulation and evaluation of effervescent tablets: a review. Journal of Drug Delivery and Therapeutics, 2018; 8: 296-303. 10.22270/jddt.v8i6.2021.
2. Fallah Huseini, H., Kianbakht, S., Hajiaghaee, R., Afkhami-Ardekani, M., Bonakdaran, A., & Dabaghian, F. H. Aloe vera leaf gel in treatment of advanced type 2 diabetes mellitus needing insulin therapy: A randomized double-blind placebo-controlled clinical trial. Journal of Medicinal Plants., 2012; 11(43): 19–27.
3. Ranade, A. N., Wankhede, S. S., Ranpise, N. S., & Mundada, M. S. Development of bilayer floating tablet of amoxicillin and Aloe vera gel powder for treatment of gastric ulcers. AAPS PharmSciTech., 2012; 13(4): 1518–1523.
4. Rahman, H., Chungath, T. T., Selvakumaraswamy, K., & Chandrasekar, R. Aloe vera mucilage as solubility enhancer in tablet formulation. Journal of Nutrition & Food Sciences, 2016; 6(5): Article 1000548.
5. Moein E, Hajimehdipoor H, Toliyat T, Choopani R, Hamzeloo-Moghadam M. Formulation of an aloe-based product according to Iranian traditional medicine and development of its analysis method. Daru., 2017; Aug 29; 25(1): 19.
6. Rao, P. B. B., Rao, A. L., Kumar, K. R., Sowmya, K., & Rao, S. K. Formulation and evaluation of eplerenone matrix tablets using Aloe vera, guar gum and povidone K-30. Pharmaceutical Journal of Sri Lanka., 2018; 8(1): 49–60.
7. Girreser U, Ugolini T, Çiçek SS. Quality control of Aloe vera (Aloe barbadensis) and Aloe ferox using band-selective quantitative heteronuclear single quantum correlation spectroscopy (bs-qHSQC). Talanta, 2019; Dec 1; 205: 120109.
8. Na K, Lkhagva-Yondon E, Kim M, Lim YR, Shin E, Lee CK, Jeon MS. Oral treatment with Aloe polysaccharide ameliorates ovalbumin-induced atopic dermatitis by restoring tight junctions in skin. Scand J Immunol, 2020 Mar; 91(3): e12856.
9. Ashwini S. Jadhav, Avani K. Shewale, Dr. Mangesh A. Bhutkar. Evaluation of Aloe vera and Hibiscus rosa-sinensis mucilage as a binder in different Tablet Formulations. Asian J. Pharm. Tech, 2020; 10(1): 29-37.
10. Jani, Girish & Shah, Dhiren & Prajapati, Vipul & Jain, Vineet. Gums and mucilages: Versatile excipients for pharmaceutical formulations. Asian Journal of Pharmaceutical Sciences, 2009; 4.
11. Irfan, J., Ali, A., Hussain, M. A., Haseeb, M. T., Naeem-ul-Hassan, M., & Hussain, S. Z. Citric acid cross-linking of a hydrogel from Aloe vera (Aloe barbadensis M.) engenders a pH-responsive, superporous, and smart material for drug delivery. RSC Advances., 2024; 14(12): 8018–8027.
12. Tevlek A, Kibar G, Cetin B. Assessment of Anticancer Effects of Aloe vera on 3D Liver Tumor Spheroids in a Microfluidic Platform. Biotechnol Bioeng, 2025; Sep; 122(9): 2592-2608.
13. Al-Mahbashi, H. M., El Shaibany, A. M., Al-Ghazali, M. A., Al-Shamahy, H. A., & Al-Ankoshy, A. A. M. Cytotoxic activities in vitro of flower extracts of three species of Aloe growing in Yemen: Aloe rubroviolaceae, Aloe vera and Aloe sabaea, against eleven types of cancer cell lines. Universal Journal of Pharmaceutical Research, 2021; 6(4): 65–71.
14. Tabolacci C, Oliverio S, Lentini A, Rossi S, Galbiati A, Montesano C, Mattioli P, Provenzano B, Facchiano F, Beninati S. Aloe-emodin as antiproliferative and differentiating agent on human U937 monoblastic leukemia cells. Life Sci., 2011 Nov 21; 89(21-22): 812-20.
15. Liu, Y., Fang, M., Tu, X., Mo, X., Zhang, L., Yang, B., Wang, F., Kim, Y. B., Huang, C., Chen, L., & Fan, S. Dietary Polyphenols as Anti-Aging Agents: Targeting the Hallmarks of Aging. Nutrients., 2024; 16(19): 3305.
16. Memorial Sloan Kettering Cancer Center. (n.d.). Aloe vera. About Herbs. Retrieved March 22, 2026; https://www.mskcc.org/cancer-care/integrative-medicine/herbs/aloe-vera.
17. Yagi A, Kabash A, Okamura N, Haraguchi H, Moustafa SM, Khalifa TI. Antioxidant, free radical scavenging and anti-inflammatory effects of aloesin derivatives in Aloe vera. Planta Med., 2002; Nov; 68(11): 957-60.
18. Li D, Wang HW, Dong AD, Zhang Q, Wang C, Wang J, Sun J, Zhao C. Extraction and purification, structural characteristics, biological activities,

applications, and quality control of Aloe vera polysaccharides: A review. Int J Biol Macromol., 2025; Nov; 329(Pt 2): 147927.
19. Yanikoglu RS, Hekimoglu R, Celikten M, Yıldız Pekoz A, Gurol AO, Esrefoglu M, Akev N, Yılmaz Ozden T, Goncu B. Anti-inflammatory potential of pre-formulated Aloe vera in mitigating allergen-induced airway responses in mice. Immunol Lett., 2025; Dec; 276: 107070.
20. Mourtzinos I, Makris DP, Yannakopoulou K, Kalogeropoulos N, Michali I, Karathanos VT. Thermal stability of anthocyanin extract of Hibiscus sabdariffa L. in the presence of beta-cyclodextrin. J Agric Food Chem., 2008; Nov 12; 56(21): 10303-10.
21. Lin, T. L., Lin, H. H., Chen, C. C., Lin, M. C., Chou, M. C., & Wang, C. J. Hibiscus sabdariffa extract reduces serum cholesterol in men and women. Nutrition Research., 2007; 27(3): 140–145.
22. Sindi, H. A. (2013). Bioactivity of anthocyanins from Hibiscus sabdariffa [Doctoral dissertation, University of Leeds]. White Rose eTheses Online.
23. Herrera-Arellano, A., Flores-Romero, S., Chávez-Soto, M. A., & Tortoriello, J. Effectiveness and tolerability of a standardized extract from Hibiscus sabdariffa in patients with mild to moderate hypertension: A controlled and randomized clinical trial. Phytomedicine., 2004; 11(5): 375–382.
24. Sinela A, Rawat N, Mertz C, Achir N, Fulcrand H, Dornier M. Anthocyanins degradation during storage of Hibiscus sabdariffa extract and evolution of its degradation products. Food Chem., 2017; Jan 1; 214: 234-241.
25. Ridzwan Krishnamurthy, Z. M., Ali, I. M., Dayoob, M., Hussein, S. S., & Khan, N. A. K. Hibiscus sabdariffa extract as anti-aging supplement through its antioxidant and anti-obesity activities. Biomedical Research and Therapy, 2020; 7(1): 3572–3578.
26. Nguyen QD, Dang TT, Nguyen TV, Nguyen TT, Nguyen NN. Microencapsulation of roselle (Hibiscus sabdariffa L.) anthocyanins: Effects of drying conditions on some physicochemical properties and antioxidant activities of spray-dried powder. Food Sci Nutr., 2021; Dec 8; 10(1): 191-203.
27. Ariestanti, D. M., Mun, A., Djajadisastra, J., Putri, R. A., Fadhila, R., & James, R. J. Exploring rosella (Hibiscus sabdariffa L.) calyx extracts as natural dye and antioxidants in lip cream product: Formulation and evaluation. Pharmaceutical Sciences and Research, 2023; 10(3): 151–161.
28. Yagi S, Uba AI, Sinan KI, Piatti D, Sagratini G, Caprioli G, Eltigani SM, Lazarova I, Zengin G. Comparative Study on the Chemical Profile, Antioxidant Activity, and Enzyme Inhibition Capacity of Red and White Hibiscus sabdariffa Variety Calyces. ACS Omega, 2023; Oct 30; 8(45): 42511-42521.
29. Idham, Zuhaili & Muhamad, Ida & Sarmidi, Mohd. Degradation kinetics and color stability of spray-dried encapsulated anthocyanins from Hibiscus sabdariffa L. Journal of Food Process Engineering, 2012; 10.1111/j.1745-4530.2010.00605.x.
30. Banwo K, Sanni A, Sarkar D, Ale O and Shetty K. Phenolics-Linked Antioxidant and Anti-hyperglycemic Properties of Edible Roselle (Hibiscus sabdariffa Linn.) Calyces Targeting Type 2 Diabetes Nutraceutical Benefits in vitro. Front. Sustain. Food Syst., 6: 660831. doi: 10.3389/fsufs.2022.660831.
31. Chiu CT, Chen JH, Chou FP, Lin HH. Hibiscus sabdariffa Leaf Extract Inhibits Human Prostate Cancer Cell Invasion via Down-Regulation of Akt/NF-kB/MMP-9 Pathway. Nutrients, 2015; Jun 24; 7(7): 5065-87.
32. Tsai MC, Chen CC, Tseng TH, Chang YC, Lin YJ, Tsai IN, Wang CC, Wang CJ. Hibiscus Anthocyanins Extracts Induce Apoptosis by Activating AMP-Activated Protein Kinase in Human Colorectal Cancer Cells. Nutrients 2023; Sep 14; 15(18): 3972.
33. Suhartika, S., & Pawitan, J. (2024). Pharmacological effect of Hibiscus sabdariffa Linn to prevent insulin resistance: A review. Journal of Medical Pharmaceutical and Allied Sciences, 13(3): 5829–5835.
34. Ahmed, A.M.A., Khalid, K.A. Anticancer properties of Roselle (Hibiscus sabdariffa L), review article 2025; Vegetos 38: 1297–1308. https://doi.org/10.1007/s42535-024-01043-7.
35. Ezcurra-Hualde M, Gómez-Leyva JF, Juarez-Curiel E, Regalado-Noyola YJ, Ardaiz N, Casares N, Ruiz-Guillamon D, Rodríguez-Leon SM, Flores-Hernández FY, Arrizabalaga L, Risson A, García-Fuentes R, Gomar C, Belsue V, Aranda F, Berraondo P, Garcia-Garcia MR. Intratumoral administration of Hibiscus sabdariffa-derived anthocyanins exerts potent antitumor effects in murine cancer models. Front Immunol., 2025; Mar 7; 16: 1549890.
36. Nogueira da Cruz ACS, Madruga Mesquita MJTA, Dantas GKR, Silva ER, Falcone De Oliveira VC, Rezende HM, Frota GM, Cavalcante M, Garcês JRC, Souza de Andrade M, Cartagenes MDSS. Applicability of Hibiscus sabdariffa L. Extract with

Anti-Inflammatory Potential in Human Health: A Review. Food Sci Nutr., 2025 Sep 23; 13(9): e70938.
37. Alburyhi MM, El-Shaibany A. Recent Innovations of Novel Drug Delivery Systems for Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules as Naturaceutical for Breast Cancer. World Journal of Pharmaceutical Research, 2024; 13(8): 1092-1112.
38. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA, Yahya TA. Drotaverine-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research, 2024; 13(18): 1285-1340.
39. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Dictyota Dichotoma Extract Medicinal Seaweed Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences, 2024; 11(4): 63-70.
40. Alburyhi MM, El-Shaibany A. Formulation and evaluation of anti-peptic ulcer capsules of Curcuma longa herbal product. World Journal of Pharmaceutical Research, 2023; 12(22): 76-96.
41. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Formulation and evaluation of polyherbal extract for skin hyperpigmentation as gel advanced delivery systems. World Journal of Pharmaceutical Research, 2024; 13(22): 1260-1280.
42. Alburyhi MM, Noman MA, Saif AA. Formulation and evaluation of natural herbal anti-acne as gel delivery systems. World Journal of Pharmaceutical Research, 2024; 13(21): 1447-1467.
43. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Formulation and evaluation of Pandanus odoratissimus L extract for treatment of nocturnal enuresis as orodispersible tablets delivery system. World Journal of Pharmaceutical Research, 2024; 13(5): 56 -71.
44. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Curcuma longa extract capsules delivery system as an advanced phytotherapy approach for cancer. European Journal of Biomedical and Pharmaceutical Sciences, 2024; 11(6): 37-43.
45. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Aloe vera extract capsules delivery system as an advanced phytotherapy approach for controlling diabetes. World Journal of Pharmacy and Pharmaceutical Sciences, 2024; 13(4): 1408-1423.
46. Alburyhi MM, El-Shaibany A. Formulation and evaluation of antitumor activity of Artemisia arborescence extract capsules as dietary supplement herbal product against breast cancer. World Journal of Pharmaceutical Research, 2024; 13(3): 95-114.
47. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. World Journal of Pharmaceutical Research, 2024; 13(8): 1052-1072.
48. Alburyhi MM, El-Shaibany A. Recent innovations of novel drug delivery systems for formulation, development and evaluation of Aloe rubroviolaceae extract capsules as naturaceutical for hepatoprotective. European Journal of Biomedical and Pharmaceutical Sciences, 2024; 11(4): 53-61.
49. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA. Meloxicam-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical and Medical Research, 2025; 11(1): 87-106.
50. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of celery extract capsules delivery system as an advanced phytotherapy approach for gout. World Journal of Pharmaceutical Research, 2024; 13(11): 2383-2404.
51. Alburyhi MM, Saif AA, Noman MA. Domperidone-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Biomedical and Pharmaceutical Sciences, 2025; 12(3): 250-269.
52. Alburyhi MM, El-Shaibany A. Formulation and evaluation of effervescent granules of Artemisia arborescence herbal product for foodborne illness. World Journal of Pharmacy and Pharmaceutical Sciences, 2023; 12(12): 1429-1444.
53. Saif AA, Alburyhi MM, Noman MA, Yahya TA, Al-Ghorafi MA. Famotidine-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research, 2024; 13(18): 1346-1408.
54. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Capsicum extract capsules delivery system as an advanced phytotherapy approach for tonic and natural stimulant. European Journal of Pharmaceutical and Medical Research, 2025; 11(6): 323-337.
55. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of chamomile extract capsules delivery system as an advanced phytotherapy approach for gout. World Journal of

Pharmaceutical and Life Sciences, 2025; 11(04): 215-228.
56. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Plicosepalus acacia extract capsules delivery system as an advanced phytotherapy approach for hepatoprotective. World Journal of Pharmaceutical Research, 2025; 14(8): 1309-1334.
57. Alburyhi MM, Noman MA, Saif AA. Metronidazole-Excipient Compatibility Studies for Medicated Chewing Gum Delivery Systems Development. European Journal of Pharmaceutical and Medical Research, 2025; 12(4): 567-589.
58. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Ginger extract capsules delivery system as an advanced phytotherapy approach for controlling diabetes. World Journal of Pharmaceutical and Medical Research, 2025; 11(6): 400-415.
59. Alburyhi MM, Saif AA, Noman MA, Al Khawlani MA. Bisoprolol-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical and Medical Research, 2024; 10(10): 304-324.
60. Alburyhi MM, Mohamed YAS, Saif AA, Noman MA. Compatibility Studies with Pharmaceutical Excipients of Amlodipine for the Development of Novel Delivery Systems. World Journal of Pharmacy and Pharmaceutical Sciences, 2024; 13(11): 95-136.
61. Alburyhi MM, Saif AA, Noman MA. Spironolactone-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences, 2025; 14(3): 871-910.
62. Alburyhi MM, Noman MA, Alemad AF. Preformulation Studies of Cefixime for Dispersible Tablets Delivery System Development. World Journal of Pharmacy and Pharmaceutical Sciences, 2024; 13(12): 75-99.
63. Alburyhi MM, Noman MA, AA Saif. Formulation and Evaluation of Meloxicam Emulgel Delivery System for Topical Applications. World Journal of Pharmaceutical Research, 2025; 14(4): 1324-1337.
64. Alburyhi MM, Saif AA, Noman MA. Ticagrelor-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences, 2024; 13(10): 1081-1132.
65. Alburyhi MM, Saif AA, Noman MA. Lornoxicam-Excipient Compatibility Studies for Microsponge-Based Drug Delivery Systems Development. World Journal of Pharmaceutical and Medical Research, 2025; 11(4): 70-81.
66. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules as Naturaceutical Novel Drug Delivery Systems for Kidney Stones. World Journal of Pharmacy and Pharmaceutical Sciences, 2024; 13(5): 1425-1443.
67. Alburyhi MM, Salim YA, Saif AA, Noman MA. Furosemide-Excipient Compatibility Studies for Advanced Drug Delivery Systems Development. World Journal of Pharmaceutical Research, 2024; 13(22): 1178-1219.
68. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Acalypha Fruticosa Extract Tablets Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical Research, 2024; 13(8): 1073-1091.
69.