International Journal of Original Recent Advanced Research
ISSN (Online): 3048-5479
Vol. 03, Issue 05, September-October 2026

DEVELOPMENT AND PHARMACEUTICAL EVALUATION OF HERBAL TRANSDERMAL PATCHES CONTAINING FICUS EXTRACT FOR ANTIDIABETIC APPLICATIONS

Deepika[1], Firoz Khan[2] Deepak Verma[3] Dr Kailash Kumar Pathak[4]

Research Scholar, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[1]

Associate Professor, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[2]

Associate Professor, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[3]

Professor/Dean, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[4]

ABSTRACT

Diabetes requires sustained glucose management, yet repeated injections and oral drug limitations motivate exploration of alternative delivery systems. Ficus species have ethnomedicinal histories and preliminary antihyperglycemic evidence, but a botanical extract is not automatically suitable for transdermal administration. This review critically integrates selected human, animal, formulation and skin-permeation literature to assess whether Ficus-containing matrix patches merit development. Small oral studies of Ficus carica and animal investigations of Ficus racemosa and Ficus bengalensis suggest biological activity, whereas a published Momordica charantia patch illustrates a related, but botanically distinct, formulation approach. These evidence streams cannot establish the efficacy of a Ficus patch. Species, plant part, extraction solvent, marker content, administration route and outcome differ substantially; therefore, no pooled effect estimate is calculated. A proposed development strategy starts with authenticated botanical material and chromatographic fingerprinting, followed by polymer screening, marker-specific release and permeation testing, mass-balance assessment, stability and dermal safety evaluation. Flux must be interpreted against an independently justified systemic dose

2026/IJORAR/01/2478

and achievable patch area. If passive delivery is inadequate, carefully evaluated enhancement or alternative delivery technologies may be considered. Future studies should connect skin permeation to systemic exposure and glycemic pharmacodynamics using appropriate controls, randomized allocation and transparent reporting, before any clinical investigation. Current evidence is exploratory and does not justify substituting an investigational herbal patch for established diabetes treatment. This narrative, meta-analysis-informed synthesis identifies critical translational gaps rather than claiming a completed systematic review or quantitative meta-analysis.

Keywords: *Ficus[1]; diabetes mellitus[2]; transdermal patch[3]; herbal extract[4]; skin permeation[5]; phytochemical standardization[6]; evidence synthesis[7].*

1. INTRODUCTION

1.1 Diabetes management and the delivery problem

Diabetes mellitus encompasses disorders of glucose regulation that can lead to cardiovascular, renal, retinal and neurological complications. Management is individualized and may include dietary support, exercise, glucose monitoring and pharmacotherapy. A delivery system that reduces administration burden could be valuable, but convenience alone does not establish a clinically useful therapy. A product must reproducibly deliver enough active substance, demonstrate meaningful glucose control, and have an acceptable risk profile in the intended population. Different phenotypes of diabetes and background treatments complicate comparisons; type 1 diabetes, in particular, requires insulin and cannot be treated by replacing it with an unvalidated botanical product. Transdermal delivery can avoid gastrointestinal degradation and initial hepatic first-pass exposure, and may provide sustained delivery with noninvasive removal [9], [27]. These benefits are conditional on reaching the circulation in therapeutically relevant amounts. Drug release from a film, movement through an artificial membrane and local retention in skin are not interchangeable with systemic absorption. Diabetes-associated skin changes, application-site variation and the possibility of local injury also make careful evaluation important. A Ficus patch should therefore be regarded as a pharmaceutical development hypothesis rather than an established antidiabetic intervention.

1.2 Ficus extracts as candidates

The genus Ficus contains many chemically distinct species. Ficus carica, the common fig, has been investigated in small human studies using oral leaf decoctions and fruit-derived preparations [1]–[3]. Ficus racemosa and Ficus bengalensis have been studied primarily using oral preparations in experimental models [5], [6]. Different botanical parts and extraction processes produce different mixtures; evidence for one species, plant part or route cannot be automatically transferred to another. In particular, the spelling F. bengalensis in some historical articles refers to the banyan commonly indexed as F. benghalensis; source nomenclature is retained in the references. Extracts may contain phenolics, flavonoids, terpenoids and other compounds, but a component's presence does not prove that it mediates a particular antidiabetic effect. Some oral effects may arise from local inhibition of carbohydrate digestion and could disappear after skin delivery. Characterizing the fraction that permeates skin, rather than only the starting extract, is essential. Marker selection should reflect chemical specificity, analytical

feasibility, stability and, where possible, biological relevance rather than relying on a nonspecific total-flavonoid value alone [26], [28].

1.3 Rationale, scope and objective

The stratum corneum provides the principal barrier to passive percutaneous delivery. The frequently cited 500-Da rule is a useful screening heuristic, not an absolute permeability law [8]. High polarity, poor solubility, strong binding to the matrix, instability and insufficient potency can limit delivery even for smaller molecules. Complex mixtures present additional difficulties because different constituents partition into the skin at different rates and may interact with the formulation. Chemical enhancers or microneedles may improve transport but bring additional safety and manufacturing requirements [10]–[13]. This review synthesizes selected past work on Ficus pharmacology, related herbal patches, skin transport and evidence appraisal. It distinguishes direct evidence from analogies and proposes a practical pathway for formulation and evaluation. Although the request specifies meta-analysis, the available examples differ in exposure route, preparations, study populations and endpoints; the present document is therefore a narrative evidence synthesis informed by meta-analytic principles, not a pooled statistical meta-analysis. Its objective is to identify what must be demonstrated before a Ficus patch could be evaluated for glycemic management.



Figure 1: Translational evidence chain for a Ficus patch.

The figure separates the evidence needed to move from a botanical observation to a clinically meaningful patch. Oral studies support initial biological plausibility but do not show that the relevant substances cross skin. Analytical work identifies measurable compounds, while release experiments show escape from a formulation rather than absorption. Skin permeation and systemic exposure must then be linked to pharmacodynamic outcomes. The final stage requires rigorous efficacy and safety testing in the intended population. Each arrow represents an unresolved translational step, not a proven relationship. The framework prevents results from a different species, preparation or route from being presented as direct evidence for a Ficus transdermal product.

2. SURVEY OF PAST WORK

Early clinical work by Serraclara and colleagues [1] investigated oral fig-leaf decoction in ten people with insulin-dependent diabetes. The report described lower postprandial glycemia and an approximately 12% lower average insulin dose during the decoction period than during a subsequent tea period. However, its small size, fixed sequence and short treatment period limit causal interpretation; changes in insulin and time effects may confound the comparison. It did not assess a transdermal formulation, and the findings should not be used to calculate a patch dose or recommend reducing prescribed insulin. A later double-blind crossover trial of F. carica leaf decoction in 28 people with type 2 diabetes reported a lower two-hour postprandial glucose value after the

decoction period, whereas changes in HbA1c were not statistically significant [2]. Crossover methods can improve precision by comparing participants with themselves, but interpretation requires reporting of sequence, washout, carryover, paired variance and concomitant medication. The short intervention also limits what HbA1c can reveal. These results support further investigation of a specific oral preparation, not proof of durable clinical benefit or equivalent effects when administered across skin.

Atkinson and colleagues [3] examined abscisic-acid-standardized fig fruit extracts in ten healthy adults in a randomized crossover study. Two higher-dose beverages reduced the glycemic index response relative to a reference glucose drink by approximately 24–25%. This observation concerns an acute oral challenge in people without diabetes and a fruit extract standardized to a particular constituent. It is not interchangeable with leaf decoction, a chronic endpoint or a skin-delivered formulation. The example nevertheless demonstrates why defining a botanical preparation by species, part, extraction and chemical content is essential. Preclinical evidence broadens the biological picture while introducing further uncertainty. Calzada and colleagues [4] investigated an aqueous F. carica leaf extract in a streptozotocin–nicotinamide mouse model and observed decreases in blood glucose under their experimental conditions, but HbA1c did not show a sustained significant reversal of chronic hyperglycemia. Tests involving carbohydrate challenges supported possible effects on digestion-related pathways. If the relevant action is mainly intestinal, delivering the preparation through skin may not reproduce it. The animal model, administered dose and extract chemistry cannot be assumed to predict human patch performance.

Hossain and colleagues [5] studied orally administered methanolic F. racemosa fruit extract in alloxan-induced diabetic mice, reporting lower blood glucose after seven days and using computational screening to nominate potential constituents. Docking predictions suggest testable hypotheses about molecular interactions; they do not establish constituent exposure, target engagement or therapeutic efficacy. The authors also noted that identified compounds were not quantified in the extract. Because fruit extract, dose and diabetic model differ from those in F. carica studies, effect sizes should not be combined merely because both plants share a genus. Gayathri and Kannabiran [6] reported glucose-related and biochemical changes after oral aqueous F. bengalensis bark extract in streptozotocin-induced diabetic rats. Another study considered aerial roots [25]. These preparations differ in species, plant part and pharmacological context from a standardized F. carica leaf patch. Other experimental reports examine F. carica leaf and bud extracts and F. racemosa fruit metabolomics [21], [22]; a review surveys F. benghalensis phytochemistry [23]. Experimental changes in oxidative stress markers or serum enzymes may accompany altered glucose, but are not substitutes for clinically meaningful glycemic outcomes. Research on diabetic neuropathy using F. racemosa [30] addresses a complication-related model and should not be interpreted as proof of systemic glycemic control.

Published transdermal research provides relevant formulation analogies. Bhujbal and colleagues [7] prepared a hydroxypropyl methylcellulose (HPMC) patch containing a fraction of Momordica charantia, not Ficus. They reported 47.59% release at six hours under their specified in vitro conditions and glucose reduction in diabetic rats. The in vitro result describes release under that study's conditions, not a predicted percentage absorbed by human skin. Animal efficacy and reported tolerability do not prove that a Ficus extract will behave similarly; nevertheless, the study illustrates the progression from film quality to permeation and pharmacodynamic assessment. Beyond diabetes, research on traditional herbal patches illustrates how analytical techniques can

identify compounds reaching the skin or a receptor compartment [24]. This distinction is crucial for multi-component extracts, because bulk extract concentration can obscure selective permeation and transformation. The chromatographic fingerprint of the donor, skin and receptor samples may differ. Putative biomarkers should be confirmed with authentic standards when available, and unknown peaks investigated using suitable mass spectrometry. The detection of a compound on the skin surface is not evidence that it enters circulation.

Conventional matrix systems disperse the extract in a polymer film that is covered by a backing layer and brought into contact with skin through an adhesive arrangement. Hydrophilic polymers such as HPMC can promote hydration and release, whereas hydrophobic polymers such as ethylcellulose may provide structural integrity or retard release. Polyvinylpyrrolidone can modify film properties and solubility. Plasticizers improve flexibility but can also change water uptake, adhesion and transport. Solvent choice and drying control are important because residual solvents, phase separation and extract degradation influence product quality. Chemical penetration enhancers can alter partitioning into skin or disrupt lipid organization, but performance depends on the permeant, concentration and formulation [10]. A higher receptor concentration accompanied by severe barrier damage may reflect irritation rather than a viable delivery strategy. Appropriate enhancer-free and blank controls help separate effects of the extract, polymer and enhancer. Microneedles bypass part of the barrier and can enable transport of otherwise poorly permeant molecules [12], [13], but insertion reliability, device integrity, microbial contamination and tissue recovery require separate assessment. Such technologies cannot be treated as a simple substitute for passive patches.

Skin models are equally consequential. Human skin obtained with consent and appropriate ethical approval is often most relevant, while porcine skin may be a practical comparator; rodent skin can overestimate human permeability. Reconstructed skin and artificial membranes have specific uses but do not necessarily replicate intact human barrier function. Franz diffusion cells allow controlled sampling of the receptor phase, provided barrier integrity, exposed area, temperature, mixing, sampling corrections and analytical recovery are documented. Flux should be reported in mass per unit area per unit time, not simply as percentage released. Herbal medicines require reproducible botanical identity and chemical quality across batches. Fingerprint analysis can reveal major compositional differences, while marker-based quantification provides numerical specifications [26], [28]. Stability of an herbal finished product is influenced by moisture, light, oxygen, packaging and interaction between constituents and excipients [29]. A single batch of dried film showing high folding endurance is therefore insufficient to support shelf life, bioequivalence or clinical performance. A stability-indicating method should measure relevant degradants as well as the selected markers; ICH stability guidance provides a general pharmaceutical framework rather than a botanical-specific validation [15].

The methodological literature provides a framework for synthesizing evidence. PRISMA 2020 describes transparent reporting of systematic reviews [14], and RoB 2, ROBINS-I and SYRCLE address distinct sources of bias in randomized, nonrandomized and animal studies [16]–[18]. Higgins and colleagues [19] explain inconsistency in meta-analysis, while GRADE considers certainty across multiple domains [20]. These instruments are not interchangeable: a laboratory release experiment needs formulation-specific quality assessment, not simply a clinical trial checklist. This review uses their concepts to highlight limitations without pretending that formal two-reviewer risk-of-bias ratings or pooled statistics were completed.



Figure 2: Proposed matrix patch and skin interface.

This schematic shows an illustrative matrix device rather than a tested Ficus product. A protective backing limits loss to the environment, and a polymer matrix holds the botanical preparation. A suitable adhesive secures the device; a removable liner protects the contact surface before use. Constituents released from the matrix must partition into and pass through the stratum corneum and viable skin before systemic uptake can occur. Each layer may affect stability, adhesion or release, so their compatibility requires testing. The picture is not to scale and does not imply that the complete extract, or any particular constituent, has demonstrated systemic absorption.

3. METHODOLOGY

This paper is a targeted narrative review with a proposed meta-analytic framework, not a completed systematic review. Literature was sought through web-accessible PubMed/Europe PMC records and publisher pages, with material consulted through 31 October 2026. Exploratory concepts included “Ficus carica diabetes,” “Ficus racemosa antidiabetic,” “herbal transdermal patch,” “skin permeation,” and “systematic review risk of bias.” The scope included selected human and animal Ficus pharmacology, an analogous botanical patch study, transdermal methodology, quality control and evidence-synthesis guidance. English-language accessible records were prioritized. There was no registered protocol, exhaustive reproducible multi-database strategy, duplicate independent screening or formal count of records. Consequently, selection and publication biases cannot be quantified, and absence of a located study must not be represented as proof that none exists. References were checked against source metadata where available; individual full texts were not uniformly reanalysed. [1]–[14].

Evidence was organized by species and plant part, formulation and route, model or population, comparator, outcome and study limitations. Direct Ficus-patch evidence would be considered separately from oral Ficus studies and non-Ficus patch analogues; the examples discussed here do not establish clinical efficacy for a Ficus patch. For a future systematic review, reviewers should preregister the question, search multiple databases and trial registries without unjustified language restrictions, document full strategies and dates, independently screen and extract data, resolve disagreements and publish the study flow. Clinical trials should be assessed using RoB 2 or ROBINS-I as appropriate, and animal intervention studies with SYRCLE; certainty for clinical outcomes can be considered using GRADE [14], [16]–[20]. Study-level means, standard deviations, sample sizes and within-person correlations in crossover studies should be extracted rather than converting p values into unsupported estimates.

A quantitative meta-analysis would be appropriate only for sufficiently comparable participants, extract identity, administration route, comparators and outcome times. For parallel trials measuring the same glycemic endpoint, calculate a mean difference in mg/dL with its standard error; convert mmol/L glucose to mg/dL by multiplying by approximately 18. For crossover trials, use the paired treatment contrast and its standard error, accounting for

carryover and period effects; do not treat periods as independent groups. If compatible comparisons are available, a random-effects model, forest plot, prediction interval and heterogeneity measures including I^2 can be considered, with sensitivity analyses by bias and preparation. Do not pool release percentages, animal glucose results and human oral-trial outcomes. There are no numerical pooled estimates, fabricated study counts or claims of statistical heterogeneity in this paper. The formulation and laboratory procedures described below are proposals, not completed experiments or established specifications.



Figure 3: Proposed formulation development sequence.

The workflow begins with botanical authentication and a documented source, followed by extraction and chemical characterization. Candidate films are then produced using a controlled experimental design rather than a single arbitrary polymer mixture. Physical quality, marker content and stability are assessed alongside release and permeation. A blank matrix and relevant controls are required to interpret the results. The final selection should balance feasible flux against skin tolerability, adhesive performance and manufacturability; maximizing release alone is not sufficient. Each box is a proposed research activity. No formulation has been prepared or tested for this review, and no numerical performance claims are implied.

4. CRITICAL ANALYSIS OF PAST WORK

The first major limitation is indirectness. Oral fig preparations have shown signals in small human studies [1]–[3], and other Ficus species have shown effects in rodents [5], [6], [25]. The delivery route determines which compounds are absorbed and whether gut-local effects contribute. An oral effective dose cannot simply be divided by patch area to predict a transdermal dose, because first-pass metabolism, skin partitioning and systemic exposure differ. Conversely, demonstrating that a marker crosses skin does not show that the marker causes glucose lowering. A biologically active permeating fraction must be identified and linked to exposure and effect.

The second limitation is biological and chemical heterogeneity. Plant part, season, geographic origin, processing, solvent, extraction yield and storage can change composition. Total phenolic content is a broad descriptor and may not identify active or toxic species. Reference standards, chromatographic fingerprints, identity testing and predefined marker ranges would improve reproducibility [26], [28]. Yet even a well-controlled chemical marker may be only a quality surrogate. Its relationship to activity must be experimentally tested, and safety-relevant constituents should also be monitored. Extraction contaminants, pesticides, microbial burden, heavy metals and residual solvents need specifications appropriate to the material and jurisdiction.

The third limitation is weak clinical inference. The 1998 study [1] included only ten participants and a fixed treatment sequence. The later crossover trial [2] was small and short, and the healthy-volunteer fruit study [3] measured acute glucose responses rather than diabetes outcomes. Postprandial glucose, fasting glucose and HbA1c differ in clinical meaning and temporal scale. Concomitant insulin and other glucose-lowering medications

may introduce confounding and hypoglycemia risk. Confidence intervals, adverse-event collection, allocation methods and prespecified outcomes should be evaluated before grading certainty; statistical significance alone is not proof of efficacy.

Fourth, animal model findings can be exaggerated or poorly transferable. Chemically induced diabetes can differ from human disease in beta-cell injury, insulin resistance and time course. Analyses should state animal numbers, sex, allocation, blinding, exclusions and exact time points. Repeated measures from the same animal are correlated and must not be counted as independent observations. A negative comparison with a standard drug does not prove equivalence unless the study is designed and powered to assess an equivalence margin. Docking scores in [5] similarly do not demonstrate target engagement in living animals.

Fifth, many formulation endpoints are proxies rather than therapeutic outcomes. A uniform film, strong folding endurance or high release from a artificial membrane does not establish penetration through intact skin. Barrier damage and receptor solvent effects may inflate results. The proper hierarchy runs from analytical recovery and release, to intact skin flux and distribution, to systemic pharmacokinetics and pharmacodynamics. The slope of cumulative mass per area versus time estimates flux only over an appropriate linear interval; short-duration permeation may not reach steady state. The proportion released must be distinguished from cumulative permeated mass and from bioavailability.

A simple dose-feasibility calculation can prevent inappropriate optimism. If a justified systemic input rate is D micrograms per hour and measured steady flux is J micrograms per square centimetre per hour, the idealized minimum area is D/J square centimetres. This screening estimate assumes stable flux, complete availability of permeant to circulation and consistent human skin conditions; it ignores lag, metabolism, adhesion loss and interindividual variation. If the required area is impractical, reformulation, enrichment, another technology or termination may be preferable. D must be supported by independent systemic exposure–response evidence, not inferred from a rodent oral dose.

Finally, incomplete safety characterization is a substantive barrier. Ficus leaf and latex exposures can cause irritation or contact reactions; photosensitization hazards and formulation-specific constituents require investigation. Extract, adhesive, enhancer and degradation products may each contribute. Skin irritation screening cannot establish absence of sensitization or repeated-dose systemic toxicity. People taking insulin or sulfonylureas could experience hypoglycemia if a biologically active product is added. Studies should document concomitant medication, adverse events, skin integrity and stopping rules, and should not enroll patients in efficacy testing until preclinical and regulatory requirements are met.



Figure 4: Proposed Franz diffusion experiment and material balance

The donor compartment holds the patch against an integrity-checked skin membrane, while the receptor compartment contains a stirred, analytically compatible medium. Samples collected over time are corrected for the amount removed and replacement dilution. A validated marker-specific assay determines cumulative permeation per exposed area; the linear portion, when present, supports estimation of steady flux and lag time. At the end, remaining marker in the patch, on the surface and in skin is measured to assess recovery. Artificial membranes may assess release but cannot establish skin permeation. Skin source, temperature, sampling, sink conditions and biological replicates must be reported.

5. DISCUSSION

A defensible development program should first select one explicitly named species and plant part. F. carica leaf is a reasonable research example because small oral human studies exist, but choosing it does not establish transdermal effectiveness. A botanist should authenticate material and deposit a voucher specimen; controlled extraction should document solvent, yield and drying. A validated HPLC or LC–MS method should quantify at least one discriminating marker and capture a broader fingerprint. Candidate markers should be prioritized by stability, permeation, safety and pharmacological relevance, while recognizing that the active principle may remain unknown. For early formulation screening, matrix films could be cast from defined combinations of HPMC and a second film-forming polymer with a controlled plasticizer concentration. A small factorial design can examine polymer ratio and plasticizer level while holding extract loading constant; enhancer concentration may be examined in a subsequent design with appropriate controls. Test film thickness and mass uniformity, content uniformity at multiple locations, tensile properties, moisture uptake, adhesive performance and residual solvent. Fourier-transform infrared spectroscopy and thermal analysis may suggest interactions, but absence of spectral changes does not prove compatibility or long-term stability.

Evaluate marker release using a suitable non-skin membrane, then measure permeation across intact human or justified surrogate skin in diffusion cells. Validate specificity, recovery and stability in receptor fluid and skin extracts; document receiver composition, surface temperature, donor area and biological replicates. Compare extract-loaded and blank patches, with and without enhancer, and include a reference formulation when meaningful. Report cumulative permeation, flux, lag time, skin retention and mass balance with uncertainty. An apparent increase in penetration should be interpreted together with barrier integrity and irritation assessments. After demonstrating feasible delivery, a controlled preclinical study should compare an active patch with a blank patch, an appropriate oral preparation and a clinically relevant pharmacological comparator where justified. Randomization, allocation concealment, blinded outcome assessment, prespecified sampling and humane endpoints strengthen inference. Plasma concentrations of permeating markers should be measured together with fasting and postprandial glucose and hypoglycemia surveillance. Skin irritation, sensitization, repeated-dose toxicity and stability require additional appropriately designed studies. Human trials would require regulatory authorization, ethical review and a rationale linking systemic exposure to benefit.

The evidence does not support an immediate clinical recommendation. Practical limitations include potentially low potency of crude extracts, differential component permeation, difficulties defining dose and batch variation. Enhancers and microneedles may increase delivery but also introduce risks, and should be adopted only when

their net benefit is demonstrated. If delivery targets cannot be achieved on a practical area without unacceptable irritation, a patch may not be viable. Patients should continue established diabetes treatment and discuss any herbal product with a qualified clinician, especially when taking medicines that can cause hypoglycemia.



Figure 5: Decision gates for translation from extract to potential clinical study

The five gates define a sequential research program, not evidence that a product has passed any stage. The botanical must first be authenticated and reproducible. Next, measured marker flux must be compared with a defensible systemic requirement and a practical application area. Subsequent studies should connect circulating exposure to a glycemic effect, then characterize dermal and systemic safety after repeated use. Only an adequate overall package can justify controlled clinical investigation. Failure at any gate should trigger redesign or discontinuation rather than automatic progression. This framework explicitly separates proposed development from clinical recommendation and highlights the uncertainty of the current evidence.

6. CONCLUSION

Ficus extracts have preliminary antidiabetic signals in selected oral human studies and experimental animal models, and botanical matrix patches have been investigated using other plants. These findings provide a rationale for research but do not demonstrate that a Ficus-containing transdermal patch can deliver an effective and safe systemic dose. Differences in species, plant parts, extraction, route, models and endpoints make a pooled numerical meta-analysis inappropriate for the evidence summarized here. Release from a film must not be confused with permeation through intact skin, systemic exposure or clinical benefit. Future work should prioritize authenticated and chemically standardized extracts, validated component-specific analytics, formulation reproducibility, intact-skin permeation, complete mass balance and exposure–response relationships. A credible dose-feasibility assessment must precede resource-intensive animal and clinical studies. Randomized and blinded preclinical designs, repeat-dose dermal and systemic safety assessment, and appropriately controlled trials are necessary before therapeutic claims. Until such evidence is available, a Ficus patch remains an investigational concept and should not replace insulin, prescribed glucose-lowering medicines or established diabetes care.

7. REFERENCES

[1] Serraclara A, Hawkins F, Pérez C, Domínguez E, Campillo JE, Torres MD, “Hypoglycemic action of an oral fig-leaf decoction in type-I diabetic patients,” Diabetes Res Clin Pract, no. 1, pp. 19-22, 1998, doi: 10.1016/s0168-8227(97)00112-5.

[2] S. Ahmadi Mazhin et al., “Ficus carica leaves decoction on glycemic factors of patients with type 2 diabetes mellitus: A double-blind clinical trial,” Jundishapur J. Nat. Pharm. Prod., vol. 11, no. 1, e25814, 2016, doi: 10.17795/jjnpp-25814.

[3] Atkinson FS, Villar A, Mulà A, Zangara A, Risco E, Smidt CR, Hontecillas R, Leber A, Bassaganya-Riera J, "Abscisic Acid Standardized Fig (Ficus carica) Extracts Ameliorate Postprandial Glycemic and Insulinemic Responses in Healthy Adults," Nutrients, no. 8, pp. E1757, 2019, doi: 10.3390/nu11081757.

[4] Calzada F, Ramírez-Santos J, Pérez-Álvarez H, Valdes M, Barbosa E, Velázquez C, "Characterizing the Antihyperglycemic Activity and Underlying Mechanisms of the Aqueous Extract of the Leaves from Ficus carica L," Molecules, no. 13, pp. 2207, 2026, doi: 10.3390/molecules31132207.

[5] Hossain MU, Rahman ABZN, Hossain MS, Dey S, Chowdhury ZM, Bhattacharjee A, Ahammad I, Hasan MK, Ahmed I, Hosen MB, Das KC, Keya CA, Salimullah M, "Harnessing animal model and computational experiments to discover antidiabetic compounds in Ficus racemosa," BMC Complement Med Ther, no. 1, pp. 215, 2025, doi: 10.1186/s12906-025-04845-7.

[6] Gayathri M, Kannabiran K, "Antidiabetic and ameliorative potential of Ficus bengalensis bark extract in streptozotocin induced diabetic rats," Indian J Clin Biochem, no. 4, pp. 394-400, 2008, doi: 10.1007/s12291-008-0087-2.

[7] Bhujbal SS, Hadawale SS, Kulkarni PA, Bidkar JS, Thatte VA, Providencia CA, Yeola RR, "A novel herbal formulation in the management of diabetes," Int J Pharm Investig, no. 4, pp. 222-226, 2011, doi: 10.4103/2230-973x.93009.

[8] Bos JD, Meinardi MM, "The 500 Dalton rule for the skin penetration of chemical compounds and drugs," Exp Dermatol, no. 3, pp. 165-169, 2000, doi: 10.1034/j.1600-0625.2000.009003165.x.

[9] Prausnitz MR, Langer R, "Transdermal drug delivery," Nat Biotechnol, no. 11, pp. 1261-1268, 2008, doi: 10.1038/nbt.1504.

[10] Williams AC, Barry BW, "Penetration enhancers," Adv Drug Deliv Rev, no. 5, pp. 603-618, 2004, doi: 10.1016/j.addr.2003.10.025.

[11] Alkilani AZ, McCrudden MT, Donnelly RF, "Transdermal Drug Delivery: Innovative Pharmaceutical Developments Based on Disruption of the Barrier Properties of the stratum corneum," Pharmaceutics, no. 4, pp. 438-470, 2015, doi: 10.3390/pharmaceutics7040438.

[12] Lim DJ, Kim HJ, "Microneedles in Action: Microneedling and Microneedles-Assisted Transdermal Delivery," Polymers (Basel), no. 8, pp. 1608, 2022, doi: 10.3390/polym14081608.

[13] Mdanda S, Ubanako P, Kondiah PPD, Kumar P, Choonara YE, "Recent Advances in Microneedle Platforms for Transdermal Drug Delivery Technologies," Polymers (Basel), no. 15, pp. 2405, 2021, doi: 10.3390/polym13152405.

[14] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D, "The

PRISMA 2020 statement: an updated guideline for reporting systematic reviews," BMJ, pp. n71, 2021, doi: 10.1136/bmj.n71.

[15] International Council for Harmonisation, "Q1A(R2): Stability testing of new drug substances and products," 2003. [Online]. Available: https://database.ich.org/sites/default/files/Q1A%28R2%29%20Guideline.pdf

[16] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT, "RoB 2: a revised tool for assessing risk of bias in randomised trials," BMJ, pp. l4898, 2019, doi: 10.1136/bmj.l4898.

[17] Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP, "ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions," BMJ, pp. i4919, 2016, doi: 10.1136/bmj.i4919.

[18] Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW, "SYRCLE's risk of bias tool for animal studies," BMC Med Res Methodol, pp. 43, 2014, doi: 10.1186/1471-2288-14-43.

[19] Higgins JP, Thompson SG, Deeks JJ, Altman DG, "Measuring inconsistency in meta-analyses," BMJ, no. 7414, pp. 557-560, 2003, doi: 10.1136/bmj.327.7414.557.

[20] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ, GRADE Working Group, "GRADE: an emerging consensus on rating quality of evidence and strength of recommendations," BMJ, no. 7650, pp. 924-926, 2008, doi: 10.1136/bmj.39489.470347.ad.

[21] El Ghouizi A, Ousaaid D, Laaroussi H, Bakour M, Aboulghazi A, Soutien RS, Hano C, Lyoussi B, "Ficus carica (Linn.) Leaf and Bud Extracts and Their Combination Attenuates Type-1 Diabetes and Its Complications via the Inhibition of Oxidative Stress," Foods, no. 4, pp. 759, 2023, doi: 10.3390/foods12040759.

[22] Liu Y, Zheng W, Zhang L, Hu L, Liu X, Cheng J, Li G, Gong M, "Metabolomics-based evidence of the hypoglycemic effect and alleviation of diabetic complications by Ficus racemosa fruit in diabetic mice," Food Funct, no. 14, pp. 7871-7884, 2022, doi: 10.1039/d2fo01163h.

[23] Ali Z, Awlqadr FH, Ali U, Ullah I, Arshad MT, Rauf A, Parveen H, Mukhtar S, Faridi U, Hossain MS, "Pharmacological and Phytochemical Insights Into Ficus benghalensis (Indian Banyan): Anti-Inflammatory, Antioxidant, and Anticancer Potentials," Food Sci Nutr, no. 6, pp. e71982, 2026, doi: 10.1002/fsn3.71982.

[24] Ma C, Sheng N, Shi G, Zhang J, Zhang T, "An efficient approach to probe the bioactive transdermal components of traditional Chinese herbal patches by UHPLC-MS: Gutong patch as a case," Phytomedicine, pp. 153776, 2021, doi: 10.1016/j.phymed.2021.153776.

[25] Singh RK, Mehta S, Jaiswal D, Rai PK, Watal G, "Antidiabetic effect of Ficus bengalensis aerial roots in experimental animals," J Ethnopharmacol, no. 1, pp. 110-114, 2009, doi: 10.1016/j.jep.2009.02.017.

[26] Noviana E, Indrayanto G, Rohman A, "Advances in Fingerprint Analysis for Standardization and Quality Control of Herbal Medicines," Front Pharmacol, pp. 853023, 2022, doi: 10.3389/fphar.2022.853023.

[27] Prausnitz MR, Mitragotri S, Langer R, "Current status and future potential of transdermal drug delivery," Nat Rev Drug Discov, no. 2, pp. 115-124, 2004, doi: 10.1038/nrd1304.

[28] Guo L, Duan L, Dou LL, Liu LL, Yang H, Liu EH, Li P, "Quality standardization of herbal medicines using effective compounds combination as labeled constituents," J Pharm Biomed Anal, pp. 320-331, 2016, doi: 10.1016/j.jpba.2016.07.023.

[29] Kim JH, Lee K, Jerng UM, Choi G, "Global Comparison of Stability Testing Parameters and Testing Methods for Finished Herbal Products," Evid Based Complement Alternat Med, pp. 7348929, 2019, doi: 10.1155/2019/7348929.

[30] Solanki ND, Bhavsar SK, "An evaluation of the protective role of Ficus racemosa Linn. in streptozotocin-induced diabetic neuropathy with neurodegeneration," Indian J Pharmacol, no. 6, pp. 610-615, 2015, doi: 10.4103/0253-7613.169579.