RESEARCH PAPER

Design and Evaluation of Starch-Based Dermal Patches from Citrullus colocynthis: A Review on Extraction and Formulation Techniques

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***Abstract*—**The transdermal drug delivery system is proving to be an alternative to the conventional dosage forms because it can provide resistance to drug release, increased patient compliance, and reduced systemic side effects. The growing demand on sustainable and biocompatible polymers has guided the studies on using natural polymers in the dermal patches compositions. Due to its biodegradability, film formation capability and transdermal suitability, starch has gained attention. Citrullus colocynthis is a medicinal plant whose therapeutic value is well known; however; recently it has been explored as a source of starch and bioactive compounds in the manufacture of pharmaceuticals. The present analysis is a critical evaluation of dermal starch patches of Citrullus colocynthisas an ingredient, paying attention to the method of starch extraction, formulation, and the criteria of evaluation. Conventional and modified methods of extraction are evaluated based on the effects they have on physicochemical characteristics and functional performance. The use of solvent casting, inclusion of plasticizers and bioactive compoundsare discussed as well as traditional methods of assessing mechanical strength, drug release properties, stability, and skin compatibility. Besides, the gaps in current research and the prospects of starch-based dermal patches development are highlighted. This review is aimed at providing a structured and systematic reference to the researcher interested in effective, reliable and non-toxic transdermal drug delivery system.

***Index Terms*—**Starch-based dermal patches, Citrullus colocynthis, transdermal drug delivery, natural polymers, starch extraction, formulation techniques.

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I. INTRODUCTION

In recent times there has been much interest in transdermal drug administration systems due to their property of delivering therapeutic agents through the skin in a controlled and non-invasive manner. Dermal patches offer many advantages over first-pass metabolism and oral and injectable dosage form, including avoiding the first-pass metabolism, increased patient adherence, continuous drug delivery, and reduced systemic side effects. As a result, immense research efforts have been channeled towards the development and improvement of dermal patches using safe, effective as well as biocompatible materials.

The use of natural polymers in the development of dermal patches has received interest in recent times because these polymers are biodegradable, biocompatible, and of low toxicity with low environmental impact [2][7]. One of the most remarkable natural polymers due to its availability, sustainability, ability to create films, and desirable mechanical properties is starch [4][9][12]. Of interest are starch-based dermal patches that can easily be modified to enhance flexibility, drug permeability and stability making them the right choice when it comes to transdermal and topical applications [1][6].

Citrullus colocynthis, alternatively called bitter apple, is a medicinal herb that was traditionally used in various medicinal practices due to its anti-inflammatory, antimicrobial, analgesic and antioxidant properties. Medicinal and therapeutic properties of different parts of the plant have been studied and recently, it has been highlighted as having potential in the provision of starch and bioactive compounds as found in nature. Citrullus colocynthis starch has good physicochemical characteristics potentially exploitable in the formulation of dermal drugs delivery.

Even though the idea of using starch as the basis of dermal patches and the medical significance of Citrullus colocynthis is gaining momentum, the available information regarding the extraction of starch in this plant and its application in the development of dermal patches remains disjointed [3][8]. Their varying extraction methods and formulation practices as well as ratings confuse any attempts to come up with a common verdict on the optimal design and efficacy [6][11][14]. Therefore, to understand the current developments, obstacles, and opportunities, it is crucial to go through the review of the current extraction and formulation procedures [2][5].

The overall purpose of this review is to review and summarize the existing literature on starch extraction of Citrullus colocynthis, the ways of constructing starch-based dermal patches, and the techniques of assessing their efficacy. This review will be aimed at creating an organized framework in the future research and development of effective, safe, and

sustainable starch-based systems of dermal patches by identifying the key findings, research challenges, and gaps.

A. Background of Transdermal Drug Delivery Systems

Purpose of the use of transdermal drug delivery systems is to provide a controlled rate of delivery of therapeutic agent through the skin and into the systemic circulation or the tissues in a localized area. The skin being the largest organ of the body is an available route to drug delivery in case proper systems are used. Dermal patches are one of the best-researched vehicle systems of transdermal delivery due to their simplicity of use, sustained release capabilities of drugs, and compliance by patients.

Compared to conventional oral and parenteral administration, the use of transdermal administration has a number of advantages, including circumventing gastrointestinal breakdown, avoiding first-pass liver metabolism, and maintaining relatively stable plasma drug concentrations [1][4][10]. Dermal patches reduce dosage schedule and minimize the changes in drug concentrations that aid in minimizing the chances of side effects [6][9]. Such advantages have stimulated significant research on the development of new materials and formulation methods to overcome such problems as limited skin permeability and uncontrolled drug absorption [2][8][15].

Advances in polymer science, formulation technology, and penetration-enhancing technologies with regard to skin penetration have enormously expanded the application of dermal patches. As a result, transdermal systems are now being explored not only in terms of systemic drug delivery but also in terms of localized therapeutic effects, including anti-inflammatory effect, analgesic effect, antimicrobial effect and wound-healing effect.

A. Natural Polymers significance in Skin Patches.

The choice of the suitable polymer plays a very important part in the design and functionality of dermal patches as it directly determines the mechanical strength, flexibility, drug release properties and compatibility with skin [4][7]. Over the last several years, natural polymers have been gaining more and more attention as alternatives to synthetic polymers due to their natural biocompatibility, biodegradability, non-toxicity, and environmental-friendly properties [2][9][12]. Such properties make natural polymers particularly most suitable to dermal and transdermal uses in drug delivery [1][6].

Natural polymers such as starch, cellulose, chitosan, and alginates are remarkably the film-forming polymers and may be modified either chemically or physically in order to improve their functional properties [3][8][14]. Their ability to interact with biological tissues positively reduces the chances of the skin being irritated, and that of allergic reaction which is crucial in the case of dermal patch formulations [5][11]. In addition, natural polymers are often cost effective and derived out of renewable sources, and this is in line with the growing demand of sustainable pharmaceutical supply [10][15].

Among the natural polymers, starch has emerged as a possible polymer of interest in the development of dermal patches due to its availability, malleability, and easy processability. Its properties of forming flexible films and addition of plasticizers and active compounds make it a viable choice of developing safe and viable skin patches. This shift of attention to the natural, plant-based polymers, in turn, has made systems based on starch one of the key research areas in the modern transdermal drug delivery.

II.LITERATUREREVIEW

Increased studies on transdermal and dermal drug delivery systems have also been done particularly owing to the growing use of natural and biodegradable polymers rather than the synthetic ones [2][7]. Most research efforts in the past focused on synthetic polymers due to their uniform quality and stability, but issues of toxicity, impact on the environment and long-term skin compatibility shifted the research to the use of plant-based polymers [5][11]. Such a change is an important benefit in the recent studies since natural polymers can be more biocompatible and acceptable by patients.

Many studies have been done on natural polymers such as starch, cellulose, and chitosan as the basis of developing dermal patches due to their ability to create a film and their use in the controlled delivery of drugs [3][8][14]. Comparative analysis reveals that starch-based films tend to exhibit better flexibility and processability than cellulose-based systems, and in addition, are cheaper than chitosan-based systems [4][9]. However, a major limitation with such studies is that standardized formulation parameters are not established and a cross-study comparison is difficult.

The recent researches have paid more attention to the medicinal plants as the source of functional polymers and bioactive substances [6][12]. Plant starches have been acquired by means of conventional wet milling, alkaline treatment, enzymatic separation, and physically stimulated techniques such as ultrasound and microwave-aided [1][10]. Studies that have discussed these techniques have shown that modified extraction processes tend to increase purity and operational efficiency of starch compared to the traditional wet extraction [7][13][15]. Indicatively, alkaline and enzymatic extractions result in starch having better film-forming properties and mechanical properties. However, such methods do often involve higher costs of processing, or can be associated with a risk of some degradation of starch granules, which is a disadvantage of methodology.

Studies that focus on the formulations all indicate significant improvements in the flexibility and drug permeability of the starch-based dermal patches upon the addition of plasticizers and penetration enhancers [2][6][9]. Polymer blending strategies have been proved to enhance mechanical stability and moisture resistance. Despite the fact that these techniques represent a major breakthrough in the formulation research, many studies evaluate only the short-term efficacy with little research conducted in terms of long-term stability and scalability. Also, varies of the nature and concentration of plasticizers among studies make it hard to compare the direct results of the studies.

Although this has been made to a major stop, the documents depict a great disparity in the strategies of extraction, formulation, and evaluation criterion [8][14]. Most of the studies focus on the usual sources of starch such as maize, potato or rice, yet research specifically focused on starch extracted out of Citrullus colocynthis is scarce [3][11]. The recent research on Citrullus colocynthis is mainly conducted in terms of its medicinal attributes rather than its use as a pharmaceutical excipient. This implies that there is a significant difference as the differences in starch structure unique to plants can have significant influences on patch effectiveness.

Also, despite being widely recognized as environmentally friendly and adaptable, other researches identify some inherent weaknesses of starch based systems, including moisture sensitivity, weakness in wet conditions, and unpredictable drug release behaviors [3][8]. Although these issues are addressed to some degree by the strategies of modification, many reports do not always gauge the trade-offs between mechanical stability, regulation of drug release, and skin compatibility. The absence of a standardized evaluation criterion also limits the reproducibility and translational ability of the current findings [6][9][13].

Overall, even the existing literature gives strong arguments supporting the feasibility of starch-based dermal patches, particularly of the plant-based ones. However, inconsistencies in extraction performance, formulation optimization and evaluation strategies highlight the need to carry out an systematic and comparative synthesis. It is essential to focus on starch obtained out of Citrullus colocynthis to advance on the existing knowledge, identify gaps in the methods, and direct the development of a standardized, efficient, and scalable system of dermal patches [5][9][15].

III. METHODOLOGY

This review employed a literature search strategy in order to identify relevant literature on starch extraction, the formulation and evaluation of dermal patches. Scopus, PubMed, Google Scholar and Web of Science were scientific databases searched using the following keywords: starch-based dermal patches, Citrullus colocynthis, natural polymers, transdermal drug delivery, and starch extraction.The articles considered were only those which were peer-reviewed and published in English. Research papers had to be found where the study was on starch extraction techniques, formulation plans or evaluation criteria of the dermal or transdermal system. Articles that were focused solely on the pharmacological activity but not relating to the formulations were excluded. The selected literature was reviewed against each other to reveal the methodological trends, strengths, weaknesses, and gaps in the research.

A. Dermal Patch Systems Dermal polymer and starch based.

Due to their favorable biological and mechanical properties, many studies have been conducted to determine the use of natural polymers in dermal and transdermal drug delivery systems. Natural polymers have been known to have the ability to form films, flexible, and compatible with the skin and thus they are the best polymers to use in formulations of dermal patches. It has been demonstrated that patches prepared using natural polymers usually exhibit increased patient compliance and reduce skin tolerance in comparison to patches prepared using synthetic polymers.

Among the biopolymers, starch in particular has been well-reported as an effective biopolymer to fabricate patches, as it is widespread, more sustainable and reshapeable [3][7]. Many studies have shown that it is possible to modify starch based films with plasticizers, cross-linking agents and combine them with other polymers to enhance mechanical strength and drug release properties [6][9][14]. Despite these advantages, starch-based dermal patches greatly depend on the type of starch, method of extraction, and mode of formulation, which leads to irregularities in the presented findings [2][8][15].

B. Methods of the Extraction and Formulation of Plant-Based Starch.

The extraction technique of starch plant resources has not been studied exhaustively and has been aimed at increasing yield, purity and functional properties. Some of the extraction methods that have been reported to influence the physicochemical properties of starch include wet milling, alkaline application, and enzymatic applications. Studies have proposed that starch derived in medicinal plants may have additional therapeutic benefits due to the existence of residual bioactive compounds.

When it comes to the dermal patch formulation, it has been shown that the starch that has been obtained must have the right film-forming capacity, mechanical strength, and the compatibility between the starch and the active pharmaceutical components [4][10]. The research on starch-based dermal patches highlights the importance of the formulation parameters such as the selection of solvent, plasticizers content, and the drying environment in affecting the efficacy of the patch [6][9][13]. Although different plant-based starches have been researched on, limited research has been done on starch derived in Citrullus colocynthis and little has been done on comparative evaluations of extraction and formulation processes [2][8][15].

Extraction Method	Key Advantage	Limitation	Reference
Wet milling	Simple and cost-effective	Lower starch purity	[6]
Alkaline extraction	Improved starch purity	Requires chemical handling	[11]

Enzymatic extraction	Preserves granule structure	Higher processing cost	[8]
Ultrasonic-assisted	Reduced extraction time	Equipment-dependent process	[12]

Table 1. Comparison of Starch Extraction Techniques Used for Dermal Patch Applications

IV. STARCH AS A BIOPOLYMER FOR DERMAL PATCHES

Starch is a polysaccharide that is naturally occurring and has become more popular in biomedical and pharmaceutical biopolymers [3][12]. Starch is a viable candidate since it is biocompatible, biodegradable and is able to form films hence can be used to make dermal patches [4][7]. Its physicochemical characteristics can be manipulated by processing and modifications and adjusted to the mechanical and functional needs of transdermal drug delivery systems [6][9][14]. Sustainable and vegetal pharmaceutical excipients will also be in demand as dermal patches using starch respond to the increasing demand [1][10].

A. Structure and Properties of Starch

Starch is made up predominantly of two polysaccharides amylose and amylopectin. Amylose is primarily linear polymer composed of 1,4 linkages and amylopectin is a considerably branched polymer containing 1,4 and 1, 6 linkages. The proportion of amylose to amylopectin is very important in determining the gelatinization properties, swelling capacity and film-forming properties of starch.

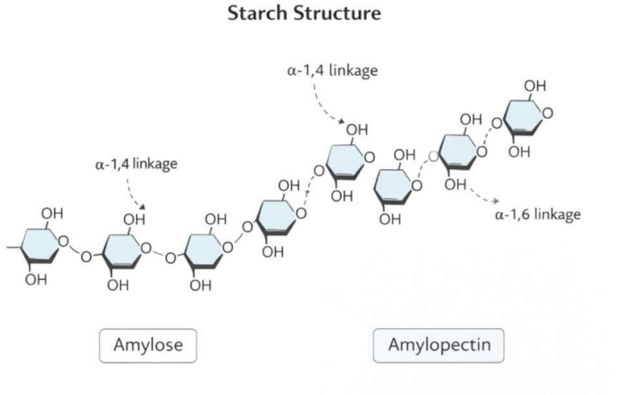

Figure 1. Molecular structure of starch showing amylose and amylopectin components.

A. Advantages of Starch in Transdermal Formulations

As a polymer in transdermal and dermal patch formula, starch has numerous advantages [4][9]. Its natural origin, as well as its non-toxicity make it more compatible with the skin and the possibility of irritation and allergy decreases [2][7][11]. Film based on starch is commercially viable and easily manufactured in straightforward and relatively inexpensive techniques like solvent casting which aids in scaling to paltry volumes [6][13].

Starch is versatile enough to deal with a broad scope of pharmaceutical compounds and excipients that are active [3][8]. It can create homogeneous films of controlled thickness allowing predictable and controlled release of drugs [1][10][14]. Further, one can also use starch in conjunction with other natural or artificial polymers to improve its mechanical properties and alter the drug permeability and hence it is a versatile material to formulate customized dermal patches [5][12][15].

B. Limitations and Modification Strategies

Although it has some benefits, the application of native starch in dermal patches formulations has some demerits. They consist of low moisture resistance, weakness and low mechanical strength in the wet climates. In addition, water trapping properties of starch can result in quickened swelling and uncontrolled bursting of drugs unless properly managed.

There are several modification strategies that have been discussed to resolve these problems [6][11]. Some of the chemical modifications that have been used to enhance stability of the mechanical properties and decrease sensitivity to water include cross-linking, esterification and etherification [3][9][14]. The physical properties have also been demonstrated to be increased to improve flexibility and resiliency such as the addition of plasticizers or other polymers [4][8]. These dermal patches that are based on starch can be enhanced by the use of such strategies to enhance their effectiveness and expand their use as pharmaceutical products [1][12][15].

V. EXTRACTION TECHNIQUES OF STARCH FROM CITRULLUS COLOSYNTHIS

The extraction of starch using the vegetative resources is crucial because it determines directly on its physicochemical properties and applicability as a pharmaceutical ingredient. In Citrullus colocynthis, starch must be extracted by means of appropriate choice of the method that can guarantee a high yield, purity and functional activity. Extraction process also influences various significant factors like integrity of the granules, moisture and crystallinity and film forming capacity and is imperative in the development of dermal patches. Some classical and altered methods of extraction have been investigated to extract starch with the desired properties to transdermal delivery system.

Figure 2. Schematic representation of starch extraction process from *Citrullus colocynthis*.

A. *A. Standard Operating Procedures of Extraction*

The traditional methods of extracting starch normally include wet grinding and separation with the use of water. In case of such techniques, a purification, grinding, and immersion of the plant material in water are performed to dissolve starch granules of the cell matrix. The slurry that arises is filtered and left to settle then separation, washing and drying of the starch is done. They are easy, inexpensive and common methods of extracting at laboratory level.

Nevertheless, traditional approaches to extraction can lead to the disproportionate purification and recovery of starch, which is influenced by such variables of the process as the time of soaking, temperature, and pH. The absence of starch removal, which is the non-starch components i.e. proteins and fibers, may result in the quality of isolated starch and constrain its use in the dermal patch preparations.

B. *B. Modified and Assisted Extraction Techniques.*

The more effective extraction methods have been designed in order to mitigate the shortcomings of the traditional methods to enhance the quality and quantity of starch [2][6]. Such methods are alkaline treatment, enzymatic extraction and physically assisted [3][9][14]. Through alkaline extraction, it is easier to remove protein material to be left with starch of higher purity and functional properties [4][11]. The enzyme processes utilize the selective action of certain enzymes to breakdown the non-starch components to leave the starch grains intact [1][8].

Different techniques have been researched to improve extraction with the help of physical force, ultrasonic, microwave-assisted extraction techniques [6][12]. The methods have the ability to enhance the transfer of the mass and help in minimizing the extraction time and solvent consumption [7][10][15]. The use of these techniques can result in starch of a more homogeneous granular size and the ability to form a film with it, which is practical in the development of dermal patches [5][9][14].

C. *C. Physicochemical Characterization of Extracted Starch*

After extraction, the starch has to be characterized in order to ascertain the appropriateness of the starch in the dermal patch development. The moisture content, swell potential, gelatinization, crystallinity and structure of the granules are some of the most commonly checked properties. These properties have an impact on mechanical strength, flexibility, and drug release properties of starch-based films.

These are physicochemical characteristics that are very much dependent on the extraction technique and source of the botanical [6][10]. Hence, starch extracted using Citrullus colocynthis should be systematically analyzed to determine the correlation that exists between the extraction processes and their workability [3][8][14]. This description forms a background of determining the right extraction methods and optimization of the formulation methods of dermal patches fabricated of starch [1][5][12].

VI. FORMULATION TECHNIQUES FOR STARCH-BASED DERMAL PATCHES

The generation of skin patches consisting of starch is one of the most important moments in the progression of the effective transdermal systems of drug delivery. The method of formulation defines the mechanical strength, flexibility, drug release properties and skin sticking properties of patch. To extract starch to be incorporated into dermal patches by a range of processes, Citrullus colocynthis can be used and the excipients are well chosen to improve its functions as well as retention. To deliver drugs and satisfaction to the patient, it is important to change the parameters of formulation.

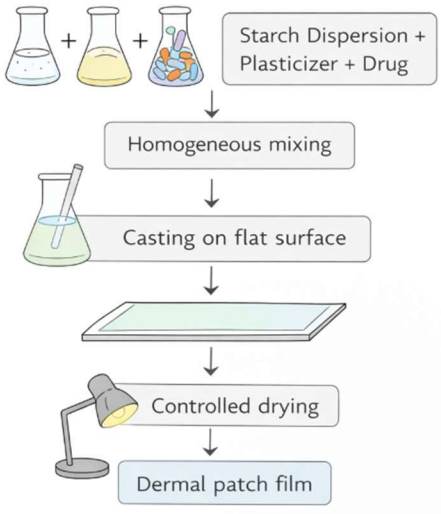

Figure 3. Schematic illustration of the solvent casting method used for preparation of starch-based dermal patches.

A. *A. Solvent Casting Method*

The most common mode of production of dermal patches of starch is through solvents casting process as a result of ease and consistency. The starch in this technique is dissolved or suspended in an appropriate mixture of solvents, and heat is often useful in facilitating the gelatinization. The polymeric solution is then developed onto a flat surface and the active ingredient and the other excipients are then added to the polymeric solution that has been erected and then dried under controlled conditions creating a uniform film.

Solvents casting method provides accuracy in the control of patch thickness, level of drug and surface regularity. Nevertheless, the choice of the solvent, drying temperature, and the conditions of the casting must be strictly regulated to avoid the presence of defects in the films and guarantee the uniformity in the performance.

B. Role of Plasticizers and Penetration Enhancers

Skin patches composed of starch need plasticizers in order to enhance flexibility and mechanical endurance. The plasticizers commonly used are the ones that lead to a decrease in intermolecular interactions in the polymer. Plasticizers have a big impact on the physical properties of the patches such as tensile strength and folding stamina depending on their nature and level.

To enhance the absorption of drugs through the skin barrier, dermal patches, which are again penetration enhancers, are normally used to promote the penetration of drugs. The action of these agents is that they modify the stratum corneum temporarily and the drug permeation increases without causing severe harm to the skin. The appropriate penetration enhancers should be chosen to make the most out of drug delivery and protect the skin.

A. C. Incorporation of Bioactive Compounds

The loading of the bioactive compounds into the dermal patches made of starch material should be well considered in providing uniformity and stability. It may be solved or dispersed in the polymer structure based on its solubility and compatibility with the starch. The interaction of the active ingredient with the polymer can affect the speed of drug release, not mentioning the overall performance of the patch.

Formulation strategies might also include the use of co-polymers or additives so as to cover delicate bioactive molecules and preserve their therapeutic actions [4][9]. Designing of formulations is important to achieve active ingredients to be released in a similar and controlled fashion and maintain the integrity of starch-based patch [1][6][12].

VII. EVALUATION PARAMETERS IN STARCH BASED DERMAL PATCHES

The use of starch-based dermal patches is a necessary procedure in determining whether these patches are suitable in transdermal and topical applications of delivery of drugs. Development that is carefully evaluated will ensure that the developed patches meet the required standards of quality, performance, and safety before further development or testing on humans. Evaluation criteria provides data about the mechanical stability, physical stability, drug dispersion, and release properties of the dermal patch.

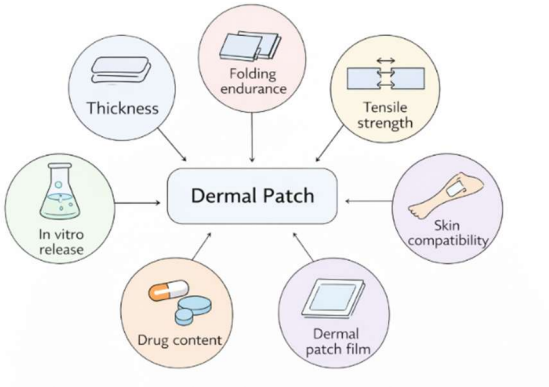

Figure 4. Key evaluation parameters used for starch-based dermal patches.

The physical analysis includes such aspects as thickness, weight stability, surface texture and visuals, which are important in ensuring consistency of a batch to another [4][9]. Constant thickness and weight indicate that there is proper blending and pouring of the polymer solution [6][12]. Folding endurance is normally measured to determine the flexibility of the patch and its ability to resist certain repeated handling processes without tearing, which is crucial because of patient usability [1][10][14].

Mechanical evaluation focuses on tensile strength, break elongation and elasticity of the patch [3][7]. These properties show the ability of the starch-based film to maintain its structural integrity during the use and wear [5][11]. The mechanical strength required in starch-based systems is also of great importance because raw starch can be brittle unless properly developed [2][8][15].

The drug evaluations include drug content uniformity assessments, in vitro drug release assessments. The homogeneous distribution of the drug on the patch ensures that the person receives the same dose every time, and in vitro experiments release tests would help to understand the release kinetics of the active ingredient in the polymer matrix. Further insight into the ability of the patch to carry the drug across the skin barrier is provided by permeation experiment with the use of proper membrane models.

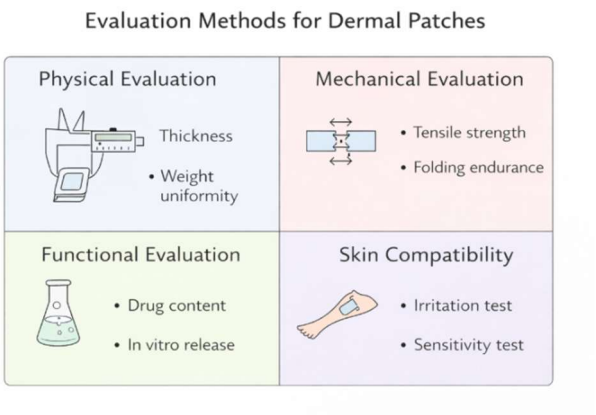

Figure 5. Categorization of evaluation methods applied to starch-based dermal patches.

Parameter	Purpose	Standard Method
Thickness	Patch uniformity	Micrometer
Tensile strength	Mechanical stability	Texture analyzer
Drug content	Dose accuracy	UV–Vis spectroscopy / HPLC
In-vitro release	Release kinetics	Franz diffusion cell
Skin irritation	Safety assessment	Patch test

Table 2. Evaluation Parameters for Starch-Based Dermal Patches

VII. STABILITY, SAFETY, AND SKIN COMPATIBILITY

The aspects that need to be taken into consideration in the formulation of dermal patches are stability, safety as well as compatibility with skin in specific cases where they are to come into prolonged contact with the skin. Stability tests are done to ascertain the physical, chemical and mechanical properties of starch based dermal patches under different storing conditions. The analyses are used in determining a possible alteration of appearance, flexibility, drug composition and release properties following a period of storage.

This may be because of climatic factors like temperature and humidity that may have a considerable impact on starch based formulations since they are susceptible to water [6][10]. Stability testing is therefore necessary since this would have ensured that the patch was still useful in the expected shelf life [3][9][14]. The changes that have been identified in stability studies present useful knowledge that can be applied in facilitating the formulation design and packaging technology [1][5][12].

The level of safety consideration is also vital particularly in formulation that gives the use of plant-based polymers and bioactive ingredients [4][11]. Dermal patches made of starch are usually highly safe, as they are of natural origin and can be identified with the biological tissues; to be sure that none of the toxic or irritating qualities are present, such substances must be tested [2][8][15]. In order to ascertain the compatibility of the patch with the human skin, experiments of skin irritation and sensitization are conducted frequently [7][13].

It has been discovered that skin compatibility does not result in any irritation or itch and neither does it result in allergy to the skins when used constantly. These reviews are significant in approving rules and consenting to patients. The safety and the stability increase the translation opportunities of the starch-based dermal patches in medical and therapeutic practice.

VIII. CHALLENGES AND RESEARCH GAPS

Although the interest in starch-based dermal patches using Citrullus colocynthis as the raw material increases, multiple challenges continue to affect the wide adoption [3][8]. The second challenge is the inconsistency of extraction of starch of plant origins [6][11]. Differences in the maturation process and extraction procedures, as well as other processing procedures, may lead to differences in starch yield, purity and functional properties [2][9][14].

Formulation problems still persist particularly how to achieve optimal mechanical strength, moisture protection and controlled drug release [4][7]. Original starch is naturally hydrophilic and this can cause excessive swelling and instability under wet conditions [1][10][15]. Although the strategies of modification have been investigated, there are more studies that should be conducted to improve on the methods without compromising on the biocompatibility [5][12].

The main gap in research is that there are no standard procedures of extraction, formulation and evaluation of starch-based dermal patches. When there are no standardized approaches, it becomes more difficult to compare the findings among studies and make conclusive formulation principles. In addition to that, most research continues to be limited in scale, i.e., laboratory level, and much has not focused on large scale manufacturing, long bead stability as well as clinical evaluation.

The reality that increased research is entailed in the dermal patches that are obtained by applying natural polymers does not create a uniform framework between the methodologies of extraction applied to starch, the methodology of formulation, and outcomes assessment, at minimum when the starch is obtained out of Citrullus colocynthis. The literature remains fragmented and has the tendency to focus either on the pharmacological action or the general properties of starch, but not on its suitability in transdermal practice. This review seals

this gap by synthesizing these areas of extraction, formulation and evaluation in methodical fashion to justify rational modeling of starch patch dermal patches.

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