BIODEGRADABLE POLYMER COMPOSITE FOR COSMETIC PATCH

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ABSTRACT: Patches has recently emerged and attracting more attention for its versatility in many areas such as cosmetic, pharmaceutical and medical. Patches can either be used to administer selected drug to skin or deliver some beneficial ingredients for cosmetic purposes. With that, as polymer is used as the matrix for patches, the polymer selected must be non-toxic, have adhesive property and non-irritative to the skin. Currently, synthetic polymer had been used as the matrix. However, as time passes, people are more concern with the environment, therefore biopolymer is chosen over synthetic polymer as they are degradable and also safe to use. Nowadays, as consumers are demanding for a more effective product that is not only good for appearance but also the health of the skin, studies had been done on many kinds of active ingredient that will give the best effect to the skin. Thus in this paper, patches made up of different combinations of polymer and active ingredients, as well as fabrication method currently used to produce patches will be discussed.

KEY WORDS: *Patche;, cosmetic; polymer; active ingredient;*

1. INTRODUCTION

A cosmetic patch is defined as an adhesive patch or film which is place above the skin to deliver a certain amount of active ingredients [1]. Delivering of active ingredients through dermal layer is better as it is safe and pain free, convenient, cheaper, and the delivery of active ingredients to the skin can be stop simply just by removing the patches [2]. The material used to make the patches can either be from synthetic polymer [3] or biopolymer [4].

Polymer is the main foundation (matrix) for a transdermal patch. The polymer use need to be stable and non-reactive, easily fabricated, exhibit excellent properties and should be able to release active ingredients consistently [2]. As mentioned above, the polymer can be either synthetic or natural based. Synthetic polymers are polyvinylchloride, polyethylene, polyvinyl alcohol and polypropylene while some example of biopolymer polymer use are cellulose derivatives, chitosan, poly caprolactone (PCL), polylactic acid (PLA) and polyglycolide (PGA) [2].

As people are becoming more concern with environmental issues, synthetic polymer is raising concern as they are non-degradable and can cause major pollution as it can remain in the environment. Therefore, bioplastics are introduced as an alternative to substitute the

conventional one as they are made from sources abundantly available in nature. To add, these polymers are also fully biodegradable, which discard the need for recycling as they will decompose in the soil. The degradation is defined by American Society for Testing of Materials (ASTM) as a modification to the chemical structure of the plastic under particular environmental condition, in which changes are characterized by the loss of mechanical and physical properties [5].

Patches have been developed mainly by the method of electrospinning as this method is well established, though electrospinning method consume high amount of voltage [6, 7, 1]. Another method that are more energy saving is solvent casting method, and many studies had also developed patches by using this method [8, 4]. Thus, this paper will be focusing on many types of patches developed with biodegradable polymer fabricated by electrospinning and solvent casting method, as to raise awareness of substituting synthetic with biodegradable polymer to help conserve the environment.

2. FABRICATION METHOD

A patch can be made or fabricated by a couple of methods, depending on the application and material used [9, 10]. Though, these two methods which are electrospinning [11-13] and solvent casting [14-16] method are widely used.

This is proven by a current research conducted by Selvi et al. [17] where they developed a metal oxide curcumin patch for wound healing using electrospinning method and obtained a fine fibre where the curcumin was incorporated in whereas for solvent casting, a polyvinyl alcohol (PVA) based patch had been developed by Engelke et al. [18] for transdermal drug delivery where the film patch formed .provided a fast release due to the weak bond between the main matrix and the active ingredient.

2.1. Electrospinning

Electrospinning is a very popular method as the end product will exhibit a porous structure and high surface area, which will make this easier to embed an active compound [19]. Based on a definition given by Jaganathan et al. [11], electrospinning is a method where a high amount of voltage is applied to a polymer solution to draw charged threads and nanofibers (diameters of hundred nanometers) are deposited at the collector end. This method is convenient in obtaining a nanofiber in the range of 100 to 1000 nm, which is a typical fiber diameter and as mentioned before, it will have small pore size and high surface area which fits to be applied in the biomedical field [20, 21].

In a recent study by Biswas et al. [13], they had developed a PLA herbal film patch by using electrospinning technique with Panchavalkala (PV) drug as the herbal active ingredient. A high voltage of 15 kV had been applied for the process and an average diameter of 100 µm had been obtained for the PLA-PV film compared to a pure PLA film which has a smaller diameter of 46 µm. Likewise, Sangnim et al. [10] had reported that voltage applied for electrospinning process significantly affect the diameters of nanofibers formed. A voltage of 5 to 25 kV was applied, and it is observed that as the voltage increased, the fiber diameter decreases.

In addition, Kim et al. [22] stated that by using electrospinning process, the placing of bioactive materials inside the nanofiber can be controlled effectively where by varying the concentration of the active ingredient affect the diameter of nanofiber patch formed. Other than that, in order to obtain a uniform and reproducible fibres, the processing conditions need to be optimized first prior to forming the patch for a study and if the optimum

conditions are achieved, a nanofiber patch with large surface area, porous and flexible structure can be obtain [6]. However, electrospinning method requires high voltage.

2.2. Solvent Casting

Solvent casting method is a very convenient method compared to electrospinning as this method does not involve any electrical device other than the magnetic stirrer required for stirring of the solution. Solvent casting is a process involving a continuous stirring of polymer blends in a chosen solvent. The solvent chose must have a solubility parameter near to the polymer. After the continuous stirring process (usually 24 hours), the blend is dried by precipitation or evaporation (in mould) in order to allow the solvent to vaporize. The final and dried mixture is a result of interfacial interaction of blend component and solvent used [8].

Many researchers had developed cosmetic patch film using solvent casting method. For instance, a chitosan/starch cosmetic patch was developed by Nisa et al. [16] and they stated that the film formed was easily removed from mold, had good colour uniformity and possess smooth surface. Doundaw et al. [9] had also developed an eudragit film patch using solvent casting method and the patch produced had a smooth surface along with transparent yellowish colour due to the active ingredients imbedded in the film. Furthermore, fabrication using solvent casting method is said to be efficient in forming the film with good uniformity of dosage unit and varied slightly. Another researcher had also reported that film produced by solvent casting technique shows good compatibility of the blended ingredients, as well as exhibiting smooth and homogenous surface [23].

Another study also developed a pectin patch using solvent casting method however patch formed was brittle therefore they incorporated deproteinized natural rubber latex (DNRL) in order to improve the flexibility of the patch [4]. Though, incorporation of DNRL actually decreases the moisture uptake and swelling ratio of the pectin patch. Other than that, Engelke et al. [18] had also chosen solvent casting method as the method is easily scalable for fabrication of film.Therefore based on all of the above reason, fabrication by solvent casting technique is highly favourable as the film produced will have homogenous smooth surface, colour uniformity and good flexibility. Table 1 summarizes researches using electrospinning and solvent casting method.

3. BIODEGRADABLE POLYMER

Researchers have been exploring vigorously on biopolymers due to diminishing of the conventional of crude oil as a raw material, and environmental pollution caused by the non-degradable petroleum based plastics. Biodegradation is defined as degradation of polymeric material solely via the enzymatic action of microorganism to produce carbon dioxide, inorganic compounds, water and biomass [24]. Biopolymers are classified into two types, those come from living organism (Natural biopolymers) and those that need to be polymerized but come from renewable sources (Synthetic biopolymers).

Table 1: Summarization of electrospinning and solvent casting methodology

Fabrication Method	Patch	Reference	Remarks
Electrospinning	PLA herbal film patch	[13]	- TEM images shows good dispersion of herbal in PLA - In vivo study shows minimum inflammation and higher targeted area contraction
	Polyurethane NF – coconut oil film patch	[11]	- FTIR analysis revealed compatibility of PU and coconut oil - Incorporation of coconut oil increase surface roughness compared to that of neat PU
	PVA tamarind seed gum patch	[10]	- Applied voltage affect diameters of NF formed - Presence of gum increase water absorbance
	PCL/Alginate NF –Spirulina film	[22]	- Alginate and spirulina help in increasing water absorbance - Patch produced shows no cytotoxicity
	Poly(D,L-lactide-co-glycolide) acid (PLGA) amoxicillin film	[6]	- Patch produce shows continuous release of amoxicillin - PLGA fibre helps in controlled released
Solvent Casting	Chitosan/starch - snail slime patch	[16]	- Patch produce have smooth surface and uniform colour
	Pectin/Nicotine patch	[4]	- Pectin patch formed is brittle, so they incorporate rubber latex to increase flexibility - Moisture uptake and swelling ratio however decrease after incorporation of rubber latex
	PVC Eudragit film patch	[9]	- Increasing active ingredients increase release rate - The film produced is deemed suitable for long term treatment
	PVA CMC film	[18]	- Incorporation of backing tape promotes fast release - Film formed has enhance water transport
	Chitosan/HPMC patch	[23]	- Good moisture uptake and swelling of patch - Patch produce shows good homogeneity

Natural biopolymers originating from living organism are found lavishly in nature such as polysaccharides, proteins and polyesters like polyhydroxyalkaonates (produced by bacteria). Polysaccharides are complex carbohydrates found in plants and animals. Plant polysaccharides include cellulose and starch. Cellulose, which is primarily linear polymer of anhydroglucose, is the amplest natural polymer on earth. The major source of cellulose is wood which contains 40–50 wt % cellulose. Cellulose is highly crystalline, fibrous, and insoluble in water [14]. Parhi and Suresh [14] had developed a hydroxypropyl methylcellulose (HPMC) patch containing cellulose where the patch formed were hard and brittle. Whereas in another study, a cellulose containing sodium alginate gave satisfactory drug release due to swellability of cellulose used [25]. From these two studies, it can be seen that incorporation of cellulose in patches gave both positive and negative effect.

On the other hand, starch has many advantages such as easy availability, biodegradability, and lower cost. Starch is the major form of stored carbohydrate in plants such as corn, rice, and potatoes. Starch is made up of a mixture of two polymers of α-glucose linear amylose and a highly branched amylopectin. Starch can also be used as a filler to produce reinforced plastics. Usually, a small amount of starch (6–30%) was compounded with synthetic polymer to increase the biodegradability of the product [5]. In patch industry, some past researchers have incorporated starch into their sample to made up a cosmetic or transdermal patch such as chitosan/starch with tamarind fruit extract and chitosan/HPMC blended patch [26, 23]. Patches obtained from both study possesses good properties in moisture uptake and compatibality with active ingredients.

Synthetic biopolymer which obtained from renewable sources and that have been extensively studied are poly-(glycolic acid) (PGA), polyhydroxyalkaonates (PHA) and polylactic acid (PLA) [2]. These types of polymers have high molecular weight and they are produced through the process of ring opening polymerization [27]. PGA is a polymer used to fabricate devices for drug delivery and tissue engineering applications. PGA is biocompatible and biodegradable, demonstrates an extensive array of erosion times, has excellent mechanical properties and most importantly, is a FDA approved polymer [28]. PHA is a family of bio-polyesters commonly develop by utilizing bacteria. They are non-toxic, biocompatible, biodegradable thermoplastics, high degree of polymerization, are highly crystalline, and are optically active. Limitations of PHA are slow biodegradation and high hydraulic stability in sterile tissues [29].

Compared to other biopolymers, PLA emerged as an attractive polymer due to its many advantages. PLA have excellent mechanical properties such semi-crystallinity, thermal stability, toughness and durability [30]. Other than that, the properties of PLA (flexibility and strength) are comparable to conventional plastics like polystyrene and polyester [31]. One distinguishable factor that makes it excellent for transdermal patches is its biocompatibility and FDA approved, making it safe for contact with skin. Moreover, a wound dressing film made up from PLA had also been proven to possess antibacterial activity [32]. Table 2 summarizes some examples of polymer used for cosmetic purposes.

Table 2: Summarization of polymers used for cosmetic purposes

Polymer	Properties	References	Remarks
Polycaprolactone (PCL)	Spirulina-PCL nanofiber – The properties of PCL allows for the fabrication of scaffolds so that the structure will not collapse during tissue formation	[33]	Usage in regeneration of dermal fibroblast layer
	Coaxial Alginate-PCL Nanofibrous Dressing – Spirulina extract was impregnated in the nanofiber without any significant bonding	[22]	Application in wound dressing
Poly vinyl alcohol (PVA)	PVA/Alginate incorporated with metal oxide curcumin - Titanium dioxide (TiO2) nanoparticles incorporated increases the wound healing property whereas curcumin can treat inflammation	[17]	Sodium alginate is a natural polymer used in many biomedical application
Chitosan and starch	Chitosan-starch with tamarind fruit extract – The best composition showed good physical properties, high water sorption and good adhesion as well as stability	[26]	Starch is obtained from tapioca
	Chitosan/HPMC blends - Blended patches produce showed good moisture uptake and patches produce is compatible with active ingredient chosen	[23]	Active ingredient is extracted from crude Z. cassumunar oil
Cellulose	Hydrophobic (Eudragit RS100) and hydrophilic (HPMC K4M) polymers – Absence of interaction between the drugs and polymer mixture through FTIR analysis	[14]	HPMC (Hydroxypropyl methylcellulose) is derived from vegetable cellulose
Xanthan Gum (Cellulose)	Sodium alginate and xanthan gum biopolymer – Satisfactory drug release due to swellability of xanthan gum	[25]	The mixture was made in order to reduce effects related to oral administration

4. ACTIVE INGREDIENTS

Active ingredient is a component in a patch that will be transferred and provide bioactive compounds for the skin. The active ingredients for cosmetic patches can be obtained from many sources, as long as the ingredients contains elements that produce beneficial effects for the skin. Some examples of active ingredients that had been use in past studies are alginate [34], fruit extract like tamarind and mulberry [26, 35] and spirulina [1].

According to Viyoch et al. [26], the active ingredients can be incorporated into the patches in two ways. The first one is by matrix type, where the active ingredient is simply dispersed in the polymer matrix. The second one is the reservoir type, where the active ingredient is placed in the reservoir in the form of solution, then is transferred by diffusion through polymer membrane. The main factor that control the rate of release of the active ingredients are the polymer designated for the patch to be develop.

4.1. Fruit Based

Many types of fruits had been used in previous studies for incorporation in the cosmetic patches. Tamarind fruit pulp extract had been used in a study previously for the development of a hydrogel patch in order to control the release of alpha-hydroxy acid, which is extracted from the tamarind fruit [26, 36]. Tamarind fruit extract is said to give a smoother and lighter colour for skin. The polymer matrix used was a crosslinked chitosan-starch, where the starch is a blend of tapioca and corn crosslinked with glutaraldehyde. Results obtained from the study was promising as the patch developed was flexible and exhibit bio-adhesive properties.

Other than incorporation in patches, tamarind seed extract had also been used in emulsion by Waqas et al. [37] to promote skin lightening and sebum control on human skin. Apart from using extract of the tamarind fruit, another researcher has incorporated tamarind seed gum into the polymer matrix of PVA [10]. Based on the results obtain, it is proven that incorporation of tamarind seed gum improved the properties of PVA as PVA/seed gum patch has higher water absorbance than a PVA only patch.

Mulberry fruit (*Morus alba* L.) is another type of fruits that are suitable to be used as an active ingredient as in the past, different parts of the mulberry plant such as root, stem and leaves had been extensively study for use of its benefits [38-40]. The extract of mulberry contains substances that can inhibit and kill acne bacteria [41]. Apart from that, extract from mulberry and its fibroin possess anti-oxidant and anti-microbial properties [42, 43].

Recently, a chitosan acne patch containing mulberry extract was developed and the patch formed shows good anti-microbial properties as it inhibited acne bacteria growth [44]. The only improvement needed for the patch produced were better strength and adhesiveness of the patch. Aside from that, Chouchan et al. [45] had also incorporated mulberry extract into a silk wound dressing patch and positive results are obtained where skin regenerated and scar less healing is promoted.

Other than that, Virgin coconut oil (VCO) obtained from a mature coconut (*Cocos nucifera*) had been widely used in many applications such as food and cosmetic owing to it benefits [11]. Such benefits are anti-inflammatory, anti-stress and anti-oxidant nature of VCO [46]. The coconut oil is usually extracted from a fresh coconut meat using enzyme-catalyzed extraction process [47].

Based on a research done by Nevin and Rajamohan [48] in the application of VCO for wound healing treatment, it is proven that wounds treated with VCO increased in pepsin soluble collagen indicating a higher collagen cross linking. Moreover after 10 days, the result shows that VCO gives anti-oxidant enzyme activities proving the various beneficial effect of VCO. Besides that, VCO had also been incorporated in the formation of biodegradable scaffolds for tissue engineering application, with scaffold produce possessing hydrophobic behaviour as well as good thermal stability [11].

4.2. Plant Based

Other than fruits, extract from plants can also be used for cosmetic purposes. For example, caffeine is another type of active ingredient that is emerging nowadays due to its many advantages. According to Herman [49], the usage of caffeine in cosmetics is increasing due to its bio-activity, ability to penetrate the skin barrier, anti-oxidant properties as well as can improve blood circulation. It is also used extensively by many researchers in order to study its capabilities and usage in many areas, along with the study on how well the caffeine is transferred through the skin itself [22, 50-52]. Marquez et al. [53] had developed a PVA caffeine composite film by a simple press molding method. Despite having weak adhesive capabilities, the film formed provide a very suitable permeation of the caffeine through the skin and the test was done by permeation assay.

Herbal extract is usually obtained from a single plant or a combination of several plant, depending on the application intended [13]. For example, "Panchavalkala" is a combination of several stem barks of trees which are *Ficusbengalensis, Ficuslacor, Ficusrecemosa, Ficusreligeosa* and *Thespesiapopulnea* [54]. Panchavalka had been used before for cleansing and dressing of wounds, and in the development of scaffold recently, scaffold produced shows good healing, minimum inflammation and faster biodegradation [13].

Apart from that, a polyherbal cosmetic cream had been developed comprising of herbal extracts such as *Glycyrrhiza glabra* root, *Piper betle* leaves and *Azadirachta indica* leaves [55] and the cream possess good antimicrobial activity. For herbal extract obtained from a single plant, one example is the aloe vera plant. Aloe vera is said to contain glycoprotein that enhance cell proliferation migration of keratinocytes, meaning that it is an effective wound healing agent [55].

In another study, a thai herb (*Zingiber cassumunar Roxb*.) was incorporated into a PVA/HPMC herbal patch for medical application [4]. The thai herb was chosen for the research because of its anti-inflammatory, anti-spasmodic herbal body and muscle treatment [56]. Based on the results obtained, the PVA/HPMC herbal patch shows a controlled release and skin permeation, as well as good mechanical properties which makes it suitable in cosmetic patch application.

4.3. Marine Based

Aside from fruits and plants, marine based compound can also be applied for cosmetic purposes based on past studies done. Alginate is one example of a marine polysaccharide that have superior capabilities such as able to retain higher amount of water compared to its weight as well as binding ion properties which stimulate the oxidative process in skin [57]. According to Paul and Sharma [58], alginate had been widely used in many applications such as in the treatment of wounds to enhance healing process, regeneration of skin cartilage [59], bone [60] and many more.

Elmotasem [61] had previously develop chitosan-alginate transdermal patch in assisting the transfer of meloxicam, an anti-inflammatory drug. The result obtained shows enhance releasing properties with the incorporation of alginate in the patch. Other than that, the study shows that the transfer of the meloxicam drug is safer through the alginate barrier instead of without it. Other than that, Kim et al. [22] had reported that incorporation of alginate into a dermal patch promote rapid release of bioactive compounds, which would be useful in the application of cosmetic as a fast release is necessary.

Among other active ingredients, spirulina shows the most promising result to be use as an active ingredient in cosmetic patch [1]. Byeon et al. [1] developed a cosmetic patch consisting of two layers, one layer being the matrix (PCL nanofiber) and the active ingredient as the second layer (spirulina extract-alginate). Spirulina was selected for this study as it contains many bioactive compounds like fatty acids and phycobiliproteins, aside from having anti-inflammatory effect and acting as an anti-oxidant. Other than that, spirulina had been used not only for development of cosmetic patch, but also other purposes such as scaffolds and wound dressing.

Byeon et al. [1] had develop a PCL patch with spirulina as the active ingredient and the produced patch gives moisturizing effect as well as containing bioactive compounds that are good for the skin. Other than that, spirulina had also been incorporated in scaffolds for medical purposes, with positive results like regeneration of dermal fibroblast layer and promotion of tissue healing [33, 62]. Another study done by Kim et al. [22] in the development of wound dressing film shows that incorporation of spirulina helps increase water uptake and bioactive release of the wound dressing film. Table 3 summarizes some applications of active ingredients used by researchers.

Though for spirulina, it is the extract which contain many bio-active compounds used in many studies. Spirulina extract contain many components and different component give different benefit as explained by Byeon et al. [1]. Phycocyanin is a common extract obtain from *Spirulina Plantesis* and is use for many purposes such as natural food dye because of its attractive blue color [24]. Past studies had been done on phycocyanin proving its anti-oxidant and anti-inflammatory effect [63-67].

Phycocyanin possess a blue colour coming from the presence of open-chain tetrapyrrole [68]. Phycocyanin is usually extracted from spirulina algae species, where a percentage of 14 % of this pigment can be obtain from a total cell protein [69]. Some conditions affect the extraction process of phycocyanin such as pH, where a stable process is obtained within the pH range of 5.0 to 7.5 and at a temperature of 9ºC, whereas at a temperature above 40ºC the process was unstable [70]. Other than that, incorporating sugar and citric acid into phycocyanin are proven to extend its shelf life and their addition is not a problem as are safe for consumption.

As Phycocyanin are proven to contain many benefits, it is widely applied in many applications such as dyes in food industry, fluorescent label and also nanotechnology [68]. In food industry, the application of phycocyanin as a natural dye replace the use of artificial dyes that are harmful to health [71]. In 2013, phycocyanin was also the first natural food dye to approved by the United States Food and Drug Administration (USFDA) to be use in the food industry [72].

It is also use as a fluorescent label because of its characteristics such as high fluorescence quantum yield and photostability, absorption and emission wavelength and high solubility in water [71, 73]. In the field of nanotechnology, phycocyanin was used in the biosynthesis of silver nanoparticles (Ag-NPs) [74]. Other than that, in nanofiber application researchers have also reported that incorporation of Phycocyanin to other compounds such as glucose increased its half-life [75].

Table 3: Summarization of active ingredients use in cosmetic, pharmaceutical and bio-medical field

Active Ingredients	Field	Purpose	Reference
Spirulina	Cosmetic	Patch (Moisturizing and bioactive effectiveness)	[1]
	Cosmetic and bio-medical	Cream (Wound healing and anti-oxidant activities)	[76]
	Bio-medical	Scaffold (Regeneration of dermal fibroblast layer)	[33]
	Bio-medical	Scaffold (Damage tissue healing)	[62]
	Bio-medical	Wound dressing (Increase water content and bio-active release)	[22]
Caffeine	Cosmetic	Patch (Anti-oxidant)	[53]
Tamarind fruit	Pharmaceutical	Patch (Topical disease treatment)	[10]
	Cosmetic	Patch (Stimulate collagen synthesis and boost skin elasticity)	[36]
Virgin Coconut oil	Bio-medical	Scaffold (Restore oxidative stress)	[11]
Herbal (Plant extract)	Cosmetic	Cream (Treatment of infectious skin disease)	[55]
	Pharmaceutical	Patch (Relief of pain and inflammation)	[23]
	Bio-medical	Scaffold (Faster wound healing)	[13]

5. CONCLUSION

Cosmetic patch (or transdermal patch) works by applying a patch onto the surface of a skin to administer a certain amount of active ingredients that will give beneficial effect to the skin. A patch should be safe and should not give irritation to the skin. Many materials had been used in the past as the main foundation for a patch such as cotton, wool, gel and plastic. Though some of this material are non-degradable hence the waste from usage of patch will cause environmental problem as they are accumulated in the landfill. Bioplastic however can solve this problem as they will degrade naturally into the environment. Other than degradability, bioplastic such as PLA, PGA and PHA are non-toxic, FDA approved and biocompatible. Apart from the main matrix, active ingredient plays an important role in cosmetic patch as it is the component that provides beneficial effect to the skin. Spirulina extract (Phycocyanin) is a component that can be incorporated as active ingredient in a patch because of its many benefits. Those benefits include bioactive compounds such as fatty acid and phycobiliprotein, anti-oxidant and anti-inflammatory effect. Furthermore, spirulina extract had been previously used in many studies such as for incorporation in scaffolds and wound dressing. As a cosmetic patch need to have a rapid release of active ingredient, alginate is a suitable addition to be used along with another active ingredient such as spirulina as alginate will help increase water uptake and release.

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