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THE SYNTHESIS OF HYDROGEL FROM SELECTIVE NATURAL RESOURCE IN MALAYSIA: A REVIEW

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ABSTRACT. *Hydrogels are hydrophilic polymer materials characterized by three-dimensional (3D) network structures that can absorb and retain significant amounts of water within their interstitial spaces. Due to their potential applications in advanced technologies across various sectors, including biomedical, pharmaceutical, biotechnology, bioseparation, biosensor, livestock, oil recovery, and cosmetics industries, hydrogels—often referred to as smart or hungry networks—are the subject of extensive scientific research. Recently, researchers have focused on creating hydrogels from natural resources to promote environmentally sustainable technologies. This review provides a concise overview of the use of oil palm empty fruit bunch (OPEFB) cellulose, C. asiatica asiaticoside, and cross-linked honey, sourced from Malaysia, in the development of hydrogels.*

KEYWORD. Hydrogel; Natural resources; Eco-Friendly Polymers; OPEFB cellulose; C. asiatica Asiaticoside; Cross-linked honey.

INTRODUCTION

Situated in the heart of Southeast Asia, Malaysia is endowed with a wealth of natural resources that underpin its vibrant and dynamic economy. The country boasts a diverse array of rich resources, including its lush rainforests and fertile agricultural lands, which yield valuable products such as palm oil, *Centella asiatica*, and honey—the latter being a prized by-product collected by bees in the expansive woodlands. As the second-largest producer of palm oil globally, Malaysia generates approximately 22–23 million tons of Oil Palm Empty Fruit Bunch (OPEFB) each year, thanks to its extensive plantations and palm oil mills (Padzil *et al*., 2020). The nation's rich biodiversity includes an abundant supply of *Centella asiatica*, commonly known as "pegaga," which plays a vital role in the ecosystem (Yusof et al., 2020). Moreover, Malaysia's lush forests are home to a variety of bee species that produce a substantial quantity of honey (Yap and Chin, 2021). This paper explores the various uses of Malaysia's natural resources, particularly their essential role in the development of hydrogels.

Hydrogels are hydrophilic polymer networks capable of absorbing significant amounts of water and undergoing swelling and shrinking. These materials have a three-dimensional (3D) network structure composed of hydrophilic polymer chains that enable them to capture and retain substantial water within their interstitial spaces (Chai et al., 2017; Ebara et al., 2014; Yuan, 2013). Hydrogels swell and form a 3D structure upon contact with water due to the presence of hydrophilic groups, such as -NH2, -OH, -COOH, and -SO3H, in their polymer networks, combined with osmotic strain (Yuan, 2013).

Crosslinking plays a crucial role in hydrogels by preventing them from dissolving in solvents while maintaining their three-dimensional structure during the swelling process. In the case of physical crosslinking, temporary connections are formed through hydrogen bonding, hydrophobic interactions, or electrostatic forces between polar groups (Rizwan et al., 2017). Conversely, smart hydrogels exhibit significant physiochemical changes in response to slight environmental variations, allowing for reversible transformations; when the triggering factor is removed, smart hydrogels can return to their original state (Ebara et al., 2014).

Smart hydrogels are advanced polymeric networks that are highly hydrated and feature intricate three-dimensional microstructures, distinguished by their ability to respond to various environmental stimuli, such as temperature, pH, light, and pressure. This responsiveness is achieved through the incorporation of stimuli-responsive co-monomers into their network architecture. Smart hydrogels boast a high degree of versatility, making them suitable for numerous applications, including drug delivery systems, optical switches, and therapeutic uses (Samal et al., 2014). The relationship between crosslinking and smart hydrogels underscores their capacity for dynamic adaptation to changing conditions, rendering them highly attractive for a wide range of applications.

2.0 CLASSIFICATION OF HYDROGEL

The classification of hydrogels is based on various factors. Hydrogels can be categorized according to their physical properties, swelling behavior, methods of preparation, origin, ionic charges, sources, biodegradation rates, and the nature of crosslinking, as illustrated in Figure 1 (Qiu and Park, 2001; Ullah et al., 2015). While this review does not delve into the specific details of each classification type, it highlights some of the key hydrogels that have garnered significant interest from researchers.

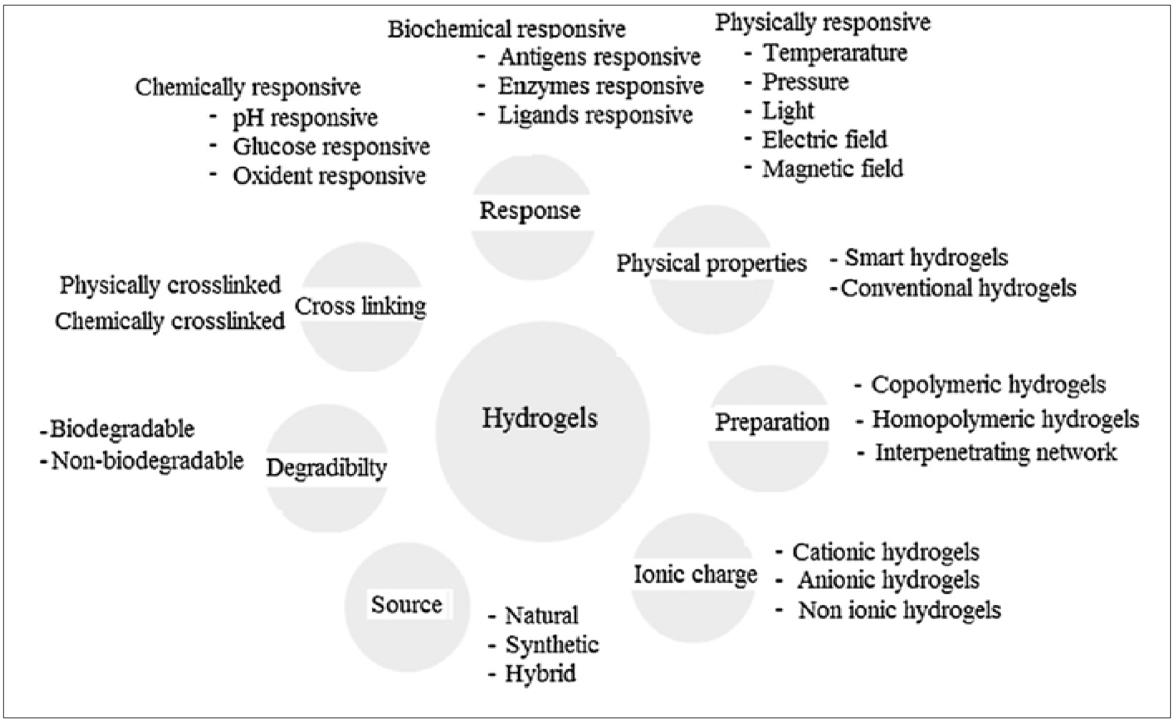

Figure 1. Classification of hydrogels based on different properties (Ullah *et al.*, 2015)

The crosslinking mechanism in physical gels is fundamentally physical in nature. Crosslinking typically occurs through processes such as hydrophobic interactions, chain aggregation, crystallization, polymer chain complexation, and hydrogen bonding (Rizwan *et al.*, 2017). In contrast, chemical hydrogels are prepared using chemical methods, such as covalent crosslinking, which can occur either simultaneously or after polymerization. Unlike chemical hydrogels, physical hydrogels are reversible due to their configurational changes.

Another type addressed in this review is the dual-network hydrogel, which is formed through electrostatic interactions by integrating both physically and chemically crosslinked hydrogels. This dual-network structure enhances the advantages of both types, offering a high capacity for liquid absorption across a broad pH range and increased sensitivity to pH variations (Qiu and Park, 2001). Recently, another variant of dual-network hydrogels has been reported, consisting of graphene polymer composites that exhibit superior mechanical properties and self-healing capabilities (Cong *et al.*, 2013).

3.0 DEVELOPMENT OF HYDROGEL

Hydrogels have emerged as versatile agents renowned for their extensive applications across biological, engineering, and medical fields. Among these, polyelectrolyte hydrogels have garnered considerable attention due to their unique capability to generate or retain charges along their polymer chains, facilitating the formation of complexes with oppositely charged species. This remarkable adaptability is widely utilized in the biological and pharmaceutical sectors (Chai *et al.*, 2017). Additionally, cationic polymers have piqued interest as they serve as synthetic carriers that can compact large structures into smaller ones while safeguarding the negatively charged DNA strands. They are employed in the creation of DNA delivery vectors, bile acid sequestration, gene therapy, and cell transfection (Qiu and Park, 2001).

In response to slight environmental variations, hydrogels can undergo substantial volume changes triggered by factors such as electric fields, solvent interactions, pH levels, ionic strength, and temperature. Current research is focused on developing hydrogels synthesized from natural resources to promote a greener environment (Salehi and Moghadam, 2023). This review provides a concise overview of the advancements in hydrogels derived from natural resources previously explored by researchers. Table 1 showcases the methods by which hydrogels were developed using selected natural resources that are readily available and abundant in Malaysia.

Table 1. Hydrogels development from selective natural resources in Malaysia.

Natural Resources	Raw Material Resources	Application	References
Oil palm empty fruit bunch (OPEFB)	Oil palm empty fruit bunch (OPEFB) are produced abundantly as a residue annually in Malaysia. About 15.8 million tonnes of Oil palm empty fruit bunch (EFB), which accounts for 20% of fresh fruit weight, are produced yearly.	The OPEFB contains up to 65% cellulose, making it a promising feedstock for cellulose extraction and manufacturing other cellulose products, such as hydrogel. Because of their enormous amount, nontoxicity, bio-compatibility, and bio-degradability, hydrogels made from natural polymers such as cellulose are excellent for use as biomaterials in the biomedical area. Cellulose-based hydrogels can be made from cellulose derivatives chemically cross-linked and dissolved in water by employing tiny bifunctional molecules as a crosslinking agent.	(Kundu *et al*., 2022) (Padzil *et al*., 2020) (Yiin *et al*., 2019) (Ng *et al*., 2015)
***Cantella asiatica* (Indian pennywort or *Asiatic* pennywort or *pegaga*).**	An herbaceous, perennial plant in the flowering plant family Apiaceae, commonly found commercially produced or plated in Malaysia. It is also grown in the open tropics, common meadows, gardens, farms, and roadsides.	Hydrogel wound dressings can benefit greatly from the addition of *Centella asiatica's Asiaticoside*, which has natural wound-healing qualities. This work investigates the in vivo performance of a hydrogel formulation high in asiaticosides that was created to promote wound healing. The outcomes demonstrate the efficacy of this strategy by demonstrating that the hydrogel rich in asiaticosides effectively promotes angiogenesis and collagen synthesis, hence expediting wound healing.	(Pinthong *et al*., 2023) (Fadzil *et al*., 2020) (Yousaf *et al*., 2020) (Sh Ahmed *et al*., 2019)

Honey	Extracted from floral nectars and other plant secretions, a carbohydrate-rich syrup prepared by honeybees. Honey is also referred to by the geographical location where the honey is produced, the honey's floral source or the trees on which the hives are located.	Studies have shown that adding multiple crosslinkers to crosslinked honey can increase its crosslinking effectiveness. Hydrogels based on alginate, encourage regenerative repair. When it combined with ghee, this mixture results in almost completely scar-free healing and has tissue thickness and build-up similar to normal skin. Additionally, honey-infused hydrogel dressings fulfil important requirements for an efficient burn wound dressing by having remarkable physical qualities like transparency, exudate absorption, and an appropriate acidic pH value.	(Pinthong *et al*., 2023) (Gope *et al*., 2022) (Ahmed and Othman, 2013) (Mohd Zohdi et al., 2012)

3.1 OPEFB Cellulose Hydrogel Development

The Oil Palm Empty Fruit Bunch (OPEFB) is a by-product generated during the processing of crude palm oil (CPO) in palm oil mills. After the fruits are separated from the fresh fruit bunches (FFB), OPEFB is collected from the empty stalks. It is estimated that for every kilogram of palm oil extracted, approximately 4 kilograms of dry biomass is produced (Abdul Khalil *et al*., 2008). In Malaysia, around 22-23 million tonnes of OPEFB are generated annually as a significant residue (Anuar *et al*., 2019). There is a growing global interest in biodegradable and environmentally friendly products, including those made from this entire production stream (Ng *et al*., 2015). Utilizing cellulose derived from OPEFB represents a promising avenue for hydrogel production. In Malaysia, OPEFB is the most affordable natural fibre available and possesses strong properties, making it widely abundant in the country. It holds great potential as an alternative primary raw material to replace woody plants. Additionally, the well-known polymeric hydrogel has attracted considerable attention due to its three-dimensional (3D) cross-linked network and high porosity (Anuar *et al*., 2019).

Despite its advantages, OPEFB-based hydrogels face several efficiency challenges, including issues with weak interfacial connectivity and mechanical strength. To address these concerns, cellulose hydrogels have been introduced. This review examines the potential of utilizing OPEFB as a cellulose source in hydrogel production within Malaysian oil palm plantations. Cellulose can be categorized into three types of nano-structured celluloses based on their processing methods. Currently, 3D printing technology is at the forefront of hydrogel production due to its ability to create complex structures and the need for high-purity products. Additionally, this review discusses some of the latest advanced applications to emphasize the strong commercialization prospects of cellulose hydrogel materials.

3.1.1 Oil Palm Empty Fruit Bunch Cellulose

Cellulose is a linear homopolymer made up of (1-4)-glycosidic bonds linking D-anhydroglucopyranose units (AGUs), as illustrated in Figure 2. Native cellulose, also known as Cellulose I, is a parallel-arranged semi-crystalline polymer and is not the most stable crystalline form (French, 2017). The natural form of cellulose is cellulose I, which consists of two structures, Iα and Iβ. The regenerated cellulose product, commonly referred to as cellulose II, has a similar molecular formula to Cellulose I (C6H10O5)n but is more stable and can be shaped into various products, including membranes, hydrogels, aerogels, and fibres (Mohammad Padzil *et al*., 2018).

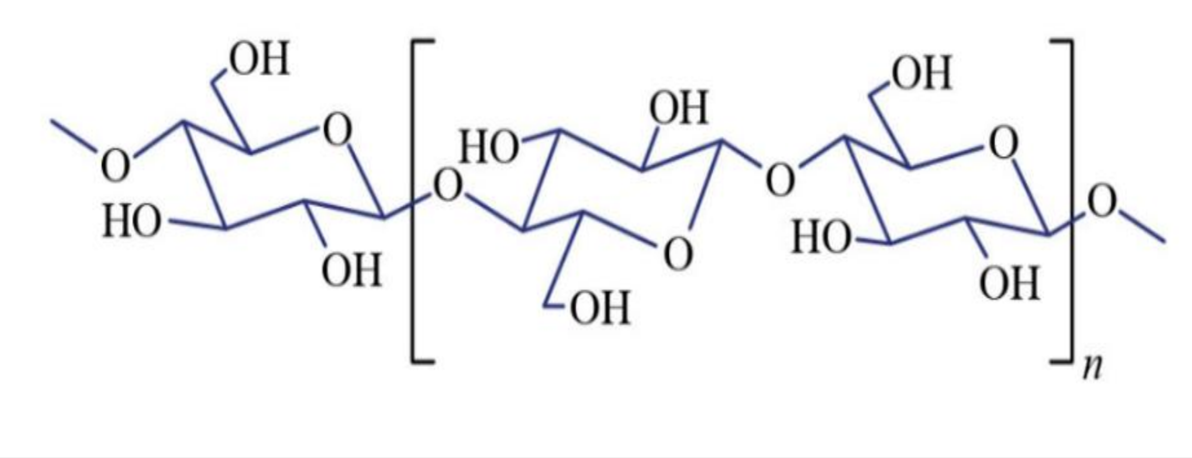

Figure 2 The cellulose structure (Britannica, 2023).

In recent years, several nanomaterials with highly promising properties have emerged, including nanocrystal cellulose (CNC or NCC), bacterial nanocellulose (BNC), and nanofiber cellulose (CNF). These nanocellulose materials are incorporated into polymers as reinforcing agents to create cellulose fibre-reinforced composites. Due to its ultralight and highly porous nature, CNF can be extracted using either chemical or mechanical methods (Gopakumar *et al*., 2020). The following subchapter will explore the potential applications of OPEFB cellulose. Various processing techniques can be employed to develop an OPEFB hydrogel, including homogenization, grafting OPEFB cellulose during the polymerization process, freeze-thaw cycles, and 3D printing technology (Athukoralalage *et al*., 2019).

3.1.2 Potential Application of OPEFB Cellulose Hydrogel

While hydrogels have been utilized across multiple sectors, only a limited number of studies have been conducted on hydrogels made from nano-sized cellulose derived from OPEFB. However, insights from prior research on cellulose-based hydrogels allow for predictions regarding the potential applications of OPEFB cellulose hydrogels. Table 2 presents the hydrogel created from OPEFB cellulose along with its possible applications.

Table 2. Potential Applications of OPEFB and Combination Materials.

Potential Application	Materials	Reference
Alternative medium for constant water supply for plants	OPEFB cellulose + NaOH/urea solvent + NaCMC	(Salleh et al., 2019)
Spikelet MCC—biocomposite, Stalk MCC—food and pharmaceutical products	Microcrystalline cellulose (MCC) extracted from OPEFB, stalks and spikelet	(Xiang et al., 2016)
Tissue engineering and medium for controlled/ slow-release fertilizer	OPEFB cellulose + NaOH/urea solvent + Sodium carboxymethylcellulose (NaCMC)	(Salleh et al., 2018)
Thermal insulating	OPEFB + graphene oxide (GO)	(Gan et al., 2018)

Source: (Padzil *et al*., 2020)

For instance, Xiang et al. (2016) investigated the suitability of microcrystalline cellulose (MCC) derived from OPEFB, including its stalks and spikelets, for use in food products. They found that the cellulose content was highest in the OPEFB stalk fibres and lowest in the spikelet fibres, which also contained the least amount of lignin and residual oil. Comparatively, the spikelet fibre MCC exhibited the highest crystallinity index among the three, suggesting it is a suitable option for load-bearing applications like biocomposites (Nafu *et al*., 2015). Hydrogels made from OPEFB stalk fibre MCC have shown performance equivalent to that of commercial MCC, indicating their potential for use in culinary and medicinal products as a substitute for commercial MCC hydrogels.

In the context of the current industrial revolution (IR4.0), additive manufacturing stands out as a key innovation in production processes. Although research on 3D printing using OPEFB nanocellulose has not yet been conducted, the demonstrated strength enhancements of OPEFB cellulose indicate significant potential for its applications in developing OPEFB nanocellulose hydrogels through 3D printing (Velasco-Hogan et al., 2018). Salleh et al. (2018) produced a regenerated superabsorbent hydrogel by dissolving OPEFB cellulose in a NaOH/urea solution along with sodium carboxymethyl cellulose (NaCMC), which may have applications in tissue engineering. Additionally, Salleh *et al*. (2019) developed a superabsorbent hydrogel leveraging the swelling capacity of OPEFB cellulose, which was found to exceed 80,000%. This type of hydrogel has the potential to maintain optimal hydration for plants. Furthermore, Gan *et al*. (2018) created an aerogel using OPEFB cellulose and graphene oxide, which featured a microporous structure and an equilibrium swelling ratio of 2000 to 3700 percent, making it potentially useful as a thermal insulating material due to its high thermal stability. The previously mentioned studies highlight the ability of OPEFB cellulose to produce superabsorbent hydrogels. Although the hydrogel produced from OPEFB nanocellulose has not yet been reported, it can be inferred that OPEFB cellulose possesses equal or even superior potential for the production of superabsorbent hydrogels suitable for various industries. OPEFB cellulose hydrogel may offer a viable solution for enhancing mechanical strength and bioactivity.

3.2 Asiaticoside-rich Hydrogel Development

Centella asiatica, commonly referred to as Indian pennywort or Asiatic pennywort, is a herbaceous, perennial plant belonging to the Apiaceae family, as depicted in Figure 3. It has traditionally been used to treat minor injuries and various ailments (Joshi and Chaturvedi, 2013). Various extracts of *Centella asiatica* and its active component, asiaticoside, have demonstrated wound-healing properties in multiple in vivo and in vitro studies (Sh Ahmed *et al*., 2019). One study focused on the in vivo effectiveness of an asiaticoside-rich hydrogel formulation in rabbits, aiming to create a formula that promotes accelerated wound healing (Ansell *et al*., 2014).

Figure 3. *Centella asiatica* (Tripathi *et al*., 2015)

3.2.1 Asiaticoside-rich Hydrogel Formulation

The aerial parts of C. asiatica were used to prepare an asiaticoside-rich fraction, which was then incorporated into a hydrogel composed of polyvinyl alcohol and polyethylene glycol (PVA/PEG) (Sh Ahmed *et al*., 2019). This hydrogel was evaluated for its wound-healing properties using an in vivo incision model. According to Sh. Ahmed *et al*. (2019), the C. asiatica PVA/PEG hydrogel was produced using the freeze-thaw technique. Initially, 8% PVA was dissolved in deionized water on a hotplate for one hour while being stirred with a magnetic stirrer. Following this, 5% PEG was added, and the mixture was autoclaved for 15 minutes at 121°C. Subsequently, 24 mg of the asiaticoside-rich fraction was dissolved in the prepared PVA/PEG hydrogel and subjected to five consecutive freeze-thaw cycles. The C. asiatica plant contains three primary compounds—asiaticoside, asiatic acid, and madecassic acid—which are formulated in the hydrogel for wound treatment (Ahmed *et al*., 2018; Ansell *et al*., 2014).

3.2.2 Asiaticoside-rich Hydrogel Potential

Centella asiatica hydrogel incorporates three key components—asiaticoside, asiatic acid, and madecassic acid—for effective wound healing. An effective wound dressing should focus on several important factors, including infection prevention, non-adherence, support for debridement, gas exchange, maintenance of wound moisture, tissue healing, and safety (Dhivya *et al*., 2015). Moreover, the wound healing process involves complex interactions among various cell types, extracellular matrix components, and cytokine mediators (Wang *et al*., 2022).

The wound-healing properties of asiaticosides may be attributed to their regulation of several mechanisms of action. Asiaticoside, in particular, has been shown to enhance antioxidant levels in the early stages of healing, which could play a crucial role in its therapeutic effects (Shukla *et al*., 1999). *C. asiatica* contains various phytochemical constituents, including sesquiterpenes, flavonoids, pentacyclic triterpenoids, plant sterols, caffeoylquinic acids, and eugenol derivatives (Gray *et al*., 2018), which contribute to its ability to maintain a moist wound environment. Given these considerations, wound dressings should also be biocompatible with tissues and blood, non-antigenic, non-toxic, and possess adequate elasticity.

As a review, it is concluded that the Asiaticoside-rich hydrogel formulated in this study is a healthy and biocompatible formulation with good physicochemical properties ideal for topical wound healing applications. Hence, biocompatible polymeric hydrogels may be the most promising wound dressing materials, as they meet the effective wound dressing requirements by providing an easy-to-handle dressing with no irritation and adhesion properties, thereby maintaining or improving patient comfort.

3.3 Cross-linked Honey Hydrogel Development

Honey is a thick, syrupy substance primarily composed of carbohydrates, produced by honeybees from the nectar of flowers (Speer et al., 2021). Its antibacterial, anti-inflammatory, and antioxidant properties are attributed to various components within honey, which also exhibit immunomodulatory effects that can aid in wound healing (Almasaudi, 2021). It is important to recognize that factors such as floral and geographic origin, extraction methods, storage conditions, and the chemical composition and quality of honey can vary by region (Lobos *et al*., 2022).

3.3.1 Cross-linked Honey Hydrogel Formulation

The formulation of honey hydrogel started with obtaining the Polyvinyl pyrrolidone (PVP) based and Polyethylene glycol (PEG), as seen in Figure 4, based on the polymer matrix. Oxoid provided the technical grade agar. Briefly, when the aqueous solution of PVP is prepared, the solution is left at room temperature (25℃) overnight. After dissolving and heating, the mixture was continuously stirred before inserting PEG. In the ultrasonic water bath, the homogenous mixture was left at 37℃, and honey was applied when the solution temperature reached below 45℃. Then, the cross-linked and sterilized electron beam (Ahmed *et al*., 2013) is performed. Thus, the cross-linked honey hydrogel is developed.

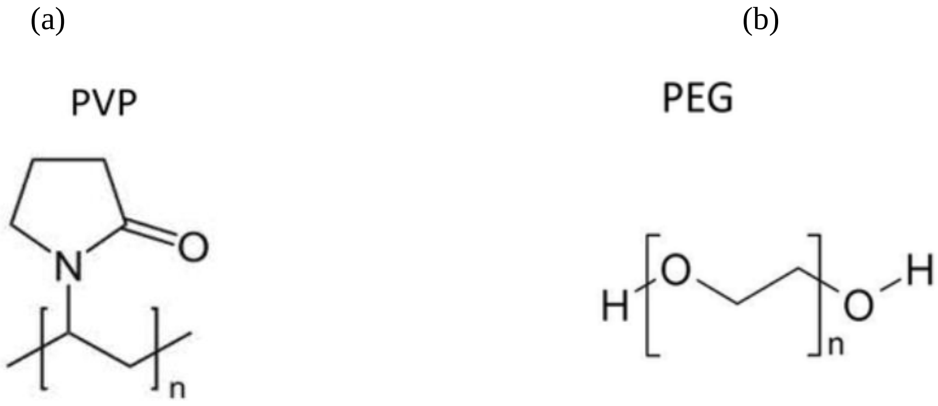

Figure 4. Structure of Polyvinyl pyrrolidone (a) and Polyethylene glycol (b) (Ramkumar *et al.*, 2016)

Studies on the development of honey hydrogels, particularly those focusing on cross-linked varieties, have yielded promising results. Researchers have explored the incorporation of polyvinyl pyrrolidone (PVP) and polyethylene glycol (PEG) as essential components of the polymer matrix to enhance the mechanical properties and bioavailability of these hydrogels (Su *et al*., 2021). When it comes to sterilization, the use of electron beam polymerization is a powerful and versatile method that can enhance the stability of hydrogels, improve crosslinking density, and boost drug incorporation capabilities. This technique facilitates tailored drug delivery and functionalized surfaces for biomaterial applications (Glass *et al*., 2019). As these advanced hydrogels continue to be the subject of ongoing research and technological advancements, they present significant potential for applications in wound healing, tissue engineering, and drug delivery.

3.3.2 Cross-linked Honey Hydrogel Potentials

Manuka honey, pasture honey, jelly bush honey, and African forest honey are well-studied varieties with documented benefits. Recently, Tualang honey (TH), a multifloral jungle honey from Malaysia, has garnered attention for its potential medicinal properties. In contrast, the advantages of Manuka honey are widely recognized across the globe (Ahmed and Othman, 2013). However, only a handful of Malaysian researchers have explored its effects in tissue culture mediums and clinical trials (Ghashm *et al*., 2010). Honey primarily consists of fructose (38%), glucose (31%), and various other sugars, along with over 180 compounds including amino acids, vitamins, minerals, and enzymes (Alnaqdy *et al*., 2005).

Malaysian honey has also demonstrated significant antibacterial properties and is effective in wound treatment. Gelam honey exhibits antioxidant and radical scavenging abilities, largely attributed to its phenolic content (Aljadi and Kamaruddin, 2004). Extracts from this honey have shown inhibitory effects on inflammatory mediators in animal models (Kassim *et al*., 2010), underscoring the considerable potential of Malaysian honey in the pharmaceutical sector. Overall, honey contributes to wound healing by alleviating common issues such as edema, inflammation, and exudation across various wound types. It promotes the proliferation of epithelial cells and fibroblasts. Manuka honey is particularly effective for treating wet burns and other types of wounds (Visavadia *et al*., 2008), and studies have indicated that Tualang honey produces similar results (Nasir *et al*., 2010).

Wounds treated with Tualang honey demonstrate a reduction in size by 32.26% for full-thickness burn wounds when compared to those treated with traditional hydrofibre silver dressings (Khoo *et al*., 2010). Patients tend to prefer Tualang honey hydrogel dressings over traditional ones due to the minimal pain experienced, the soothing effects of the treatment, and the pleasant fragrance of the dressings (Imran *et al*., 2011). Moreover, certain microorganisms are sensitive to specific types of honey. The table below provides a comparative list of microorganisms that are susceptible to both Tualang and Manuka honey.

Table 3. List of microorganisms found to be susceptible to the honey of Tualang and Manuka

Gram-positive strains		**Gram-negative strains**	
Tualang honey	**Manuka honey**	**Tualang honey**	**Manuka honey**
Streptococcus pyogenes	*Streptococcus pyogenes*	*Stenotrophomonas maltophilia*	*Stenotrophomonas maltophilia*
Coagulase-negative Staphylococci	*Coagulase-negative Staphylococci*	*Acinetobacter baumannii*	*Acinetobacter baumannii*
Methicillin-resistant - Staphylococcus aureus (MRSA)	*Methicillin-resistant - Staphylococcus aureus (MRSA)*	*Salmonella enterica Serovar typhi*	*Salmonella enterica Serovar typhi*
Streptococcus agalactiae	*Streptococcus agalactiae*	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*
Staphylococcus aureus	*Staphylococcus aureus*	*Proteus mirabilis*	*Proteus mirabilis*
Coagulase-negative-Staphylococcus aureus (CONS)	*Coagulase-negative-Staphylococcus aureus (CONS)* - haemolytic streptococci - *Enterococcus* - *Streptococcus mutans* - *Streptococcus sobrinus* - *Actinomyces viscosus*	*Shigella flexneri*	*Shigella flexneri*
		Escherichia coli	*Escherichia coli*
		Enterobacter cloacae	*Enterobacter cloacae*
		Shigella sonnei	*Shigella sonnei*
		Salmonella typhi	*Salmonella typhi*
		Klebsiella pneumonia	*Klebsiella pneumonia*

	Stenotrophomonas maltophilia	***Stenotrophomonas maltophilia***
		Burkholderia cepacia
		Helicobacter pylori
		Campylobacter spp.
		Porphyromonas gingivalis

Source: Department of Pathology, USM

While Manuka honey is globally recognized for its therapeutic properties, Malaysian honey, particularly Tualang honey, has recently garnered attention for its significant potential in tissue culture, clinical trials, and wound healing applications. These honeys are increasingly valued in the pharmaceutical industry due to their remarkable antibacterial and anti-inflammatory properties, along with their rich presence of bioactive compounds. As further research uncovers their unique benefits, the use of these natural substances may expand, paving the way for innovative approaches to wound care and other areas, thus providing patients with soothing and effective treatment options.

CONCLUSION

Hydrogels are renowned for their ability to absorb water and have a wide range of applications across various fields, making them a focal point of scientific research. Researchers are actively working to develop hydrogels using plentiful Malaysian natural resources such as C. asiatica asiaticoside, cellulose from oil palm empty fruit bunch (OPEFB), and cross-linked honey, aiming to create environmentally sustainable solutions that leverage Malaysia's abundant natural wealth. This selection of resources reflects a strong commitment to resource conservation and eco-friendly technology, paving the way for the development of "green" technologies and innovative products in the rapidly evolving hydrogel research field. By utilizing these renewable resources, researchers can meet market demands for novel materials while promoting the responsible use of advanced technologies. The progress made in natural resource hydrogel research opens up new possibilities for environmentally conscious scientific investigations and applications across various industries. Ultimately, this integration of sustainable practices with scientific research will shape the future of hydrogel applications and their broader implications.

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REFERENCES

Abdul Khalil, H., Siti Alwani, M., Ridzuan, R., Kamarudin, H. & Khairul, A. 2008. Chemical composition, morphological characteristics, and cell wall structure of Malaysian oil palm fibers. *Polymer-Plastics Technology and Engineering,* 47**,** 273-280.

Ahmed, A. S., Mandal, U. K., Taher, M., Susanti, D. & Jaffri, J. M. 2018. PVA-PEG physically cross-linked hydrogel film as a wound dressing: experimental design and optimization. *Pharmaceutical development and technology,* 23**,** 751-760.

Ahmed, S. & Othman, N. H. 2013. Review of the medicinal effects of tualang honey and a comparison with manuka honey. *The Malaysian journal of medical sciences: MJMS,* 20**,** 6.

Aljadi, A. & Kamaruddin, M. 2004. Evaluation of the phenolic contents and antioxidant capacities of two Malaysian floral honeys. *Food chemistry,* 85**,** 513-518.

Almasaudi, S. 2021. The antibacterial activities of honey. *Saudi Journal of Biological Sciences,* 28**,** 2188-2196.

Alnaqdy, A., Al-Jabri, A., Al Mahrooqi, Z., Nzeako, B. & Nsanze, H. 2005. Inhibition effect of honey on the adherence of Salmonella to intestinal epithelial cells in vitro. *International journal of food microbiology,* 103**,** 347-351.

Ansell, D. M., Campbell, L., Thomason, H. A., Brass, A. & Hardman, M. J. 2014. A statistical analysis of murine incisional and excisional acute wound models. *Wound Repair and Regeneration,* 22**,** 281-287.

Anuar, N. I. S., Zakaria, S., Gan, S., Chia, C. H., Wang, C. & Harun, J. 2019. Comparison of the morphological and mechanical properties of oil Palm EFB fibres and kenaf fibres in nonwoven reinforced composites. *Industrial Crops and Products,* 127**,** 55-65.

Athukoralalage, S. S., Balu, R., Dutta, N. K. & Roy Choudhury, N. 2019. 3D bioprinted nanocellulose-based hydrogels for tissue engineering applications: A brief review. *Polymers,* 11**,** 898.

Britannica, T. E. O. E. 2023. Cellulose. *In:* CELLULOSE (ed.). Encyclopedia Britannica.

Chai, Q., Jiao, Y. & Yu, X. 2017. Hydrogels for biomedical applications: their characteristics and the mechanisms behind them. *Gels,* 3**,** 6.

Cong, H.-P., Wang, P. & Yu, S.-H. 2013. Stretchable and self-healing graphene oxide–polymer composite hydrogels: a dual-network design. *Chemistry of Materials,* 25**,** 3357-3362.

Dhivya, S., Padma, V. V. & Santhini, E. 2015. Wound dressings–a review. *BioMedicine,* 5**,** 22.

Ebara, M., Kotsuchibashi, Y., Narain, R., Idota, N., Kim, Y.-J., Hoffman, J. M., Uto, K., Aoyagi, T., Ebara, M. & Kotsuchibashi, Y. 2014. Smart hydrogels. *Smart biomaterials***,** 9-65.

Fadzil, N., Abu Bakar, M., Yusop, M. & Abu Bakar, F. 2020. Sensorial and physicochemical characteristics of herbal noodle enriched with Centella asiatica. *Food Research,* 4**,** 1030-1037.

French, A. D. 2017. Glucose, not cellobiose, is the repeating unit of cellulose and why that is important. *Cellulose,* 24**,** 4605-4609.

Gan, S., Zakaria, S., Chia, C. H. & Kaco, H. 2018. Effect of graphene oxide on thermal stability of aerogel bio-nanocomposite from cellulose-based waste biomass. *Cellulose,* 25**,** 5099-5112.

Ghashm, A. A., Othman, N. H., Khattak, M. N., Ismail, N. M. & Saini, R. 2010. Antiproliferative effect of Tualang honey on oral squamous cell carcinoma and osteosarcoma cell lines. *BMC complementary and alternative medicine,* 10**,** 1-8.

Glass, S., Kühnert, M., Abel, B. & Schulze, A. 2019. Controlled electron-beam synthesis of transparent hydrogels for drug delivery applications. *Polymers,* 11**,** 501.

Gopakumar, D. A., Thomas, S., Owolabi, F., Thomas, S., Nzihou, A., Rizal, S. & Khalil, H. A. 2020. Nanocellulose based aerogels for varying engineering applications. *Encyclopedia of renewable and sustainable materials,* 2**,** p. 155-165.

Gope, A., Mukhopadhyay, A., Mukhopadhyay, O. & Chatterjee, J. 2022. Regenerative repair of full thickness skin wound assisted by dual crosslinking percolative gel casting maneuvered alginate hydrogel embedded with honey ghee blend resembles standard cutaneous properties. *Journal of Tissue Viability,* 31**,** 657-672.

Gray, N. E., Alcazar Magana, A., Lak, P., Wright, K. M., Quinn, J., Stevens, J. F., Maier, C. S. & Soumyanath, A. 2018. Centella asiatica: phytochemistry and mechanisms of neuroprotection and cognitive enhancement. *Phytochemistry Reviews,* 17**,** 161-194.

Imran, F.-H., Dorai, A. A., Halim, A. S. & Sulaiman, W. A. W. 2011. Tualang honey hydrogel in the treatment of split-skin graft donor sites. *Journal of ApiProduct and ApiMedical Science,* 3**,** 33-37.

Joshi, K. & Chaturvedi, P. 2013. Therapeutic efficiency of Centella asiatica (L.) Urb. An underutilized green leafy vegetable: an overview. *International Journal of Pharma and Bio Sciences,* 4**,** 135-149.

Kassim, M., Achoui, M., Mansor, M. & Yusoff, K. M. 2010. The inhibitory effects of Gelam honey and its extracts on nitric oxide and prostaglandin E2 in inflammatory tissues. *Fitoterapia,* 81**,** 1196-1201.

Khoo, Y.-T., Halim, A. S., Singh, K.-K. B. & Mohamad, N.-A. 2010. Wound contraction effects and antibacterial properties of Tualang honey on full-thickness burn wounds in rats in comparison to hydrofibre. *BMC Complementary and Alternative Medicine,* 10**,** 1-8.

Kundu, R., Mahada, P., Chhirang, B. & Das, B. 2022. Cellulose hydrogels: Green and sustainable soft biomaterials. *Current Research in Green and Sustainable Chemistry,* 5**,** 100252.

Lobos, I., Silva, M., Ulloa, P. & Pavez, P. 2022. Mineral and botanical composition of honey produced in Chile's Central-Southern region. *Foods,* 11**,** 251.

Mohammad Padzil, F. N., Gan, S., Zakaria, S., Mohamad, S. F., Mohamed, N. H., Seo, Y. B. & Ellis, A. V. 2018. Increased solubility of plant core pulp cellulose for regenerated hydrogels through electron beam irradiation. *Cellulose,* 25**,** 4993-5006.

Mohd Zohdi, R., Abu Bakar Zakaria, Z., Yusof, N., Mohamed Mustapha, N. & Abdullah, M. N. H. 2012. Gelam (Melaleuca spp.) honey-based hydrogel as burn wound dressing. *Evidence-Based Complementary and Alternative Medicine,* 2012.

Nafu, Y. R., Foba-Tendo, J., Njeugna, E., Oliver, G. & Cooke, K. O. 2015. Extraction and characterization of fibres from the stalk and spikelets of empty fruit bunch. *Journal of Applied Chemistry,* 2015**,** 1-10.

Nasir, N.-A. M., Halim, A. S., Singh, K.-K. B., Dorai, A. A. & Haneef, M.-N. M. 2010. Antibacterial properties of tualang honey and its effect in burn wound management: a comparative study. *BMC Complementary and Alternative Medicine,* 10**,** 1-7.

Ng, P., Chia, C. H., Zakaria, S., Gan, S., Kaco, H., Padzil, F. N. M. & Chook, S. W. 2015. Preparation of cellulose hydrogel from oil palm empty fruit bunch fibers cellulose. *Polymers Research Journal,* 9**,** 449.

Padzil, F. N. M., Lee, S. H., Ainun, Z. M. A. A., Lee, C. H. & Abdullah, L. C. 2020. Potential of oil palm empty fruit bunch resources in nanocellulose hydrogel production for versatile applications: A review. *Materials,* 13**,** 1245.

Pinthong, T., Yooyod, M., Daengmankhong, J., Tuancharoensri, N., Mahasaranon, S., Viyoch, J., Jongjitwimol, J., Ross, S. & Ross, G. M. 2023. Development of Natural Active Agent-Containing Porous Hydrogel Sheets with High Water Content for Wound Dressings. *Gels,* 9**,** 459.

Qiu, Y. & Park, K. 2001. Environment-sensitive hydrogels for drug delivery. *Advanced drug delivery reviews,* 53**,** 321-339.

Ramkumar, P., Kulkarni, D. M. & Waigaonkar, S. D. 2016. Macro Level Investigation On Thickness Variation Of Rot Moulded Lldpe Product. *Advanced Polymeric Materials: From Macro-to Nano-Length Scales***,** 121.

Rizwan, M., Yahya, R., Hassan, A., Yar, M., Azzahari, A. D., Selvanathan, V., Sonsudin, F. & Abouloula, C. N. 2017. pH sensitive hydrogels in drug delivery: Brief history, properties, swelling, and release mechanism, material selection and applications. *Polymers,* 9**,** 137.

Salehi, M. B. & Moghadam, A. M. 2023. Sustainable production of hydrogels. *Sustainable Hydrogels.* Elsevier.

Salleh, K. M., Zakaria, S., Sajab, M. S., Gan, S., Chia, C. H., Jaafar, S. N. S. & Amran, U. A. 2018. Chemically crosslinked hydrogel and its driving force towards superabsorbent behaviour. *International journal of biological macromolecules,* 118**,** 1422-1430.

Salleh, K. M., Zakaria, S., Sajab, M. S., Gan, S. & Kaco, H. 2019. Superabsorbent hydrogel from oil palm empty fruit bunch cellulose and sodium carboxymethylcellulose. *International journal of biological macromolecules,* 131**,** 50-59.

Samal, S. K., Dash, M., Dubruel, P. & Van Vlierberghe, S. 2014. Smart polymer hydrogels: properties, synthesis and applications. *Smart polymers and their applications.* Elsevier.

Sh Ahmed, A., Taher, M., Mandal, U. K., Jaffri, J. M., Susanti, D., Mahmood, S. & Zakaria, Z. A. 2019. Pharmacological properties of Centella asiatica hydrogel in accelerating wound healing in rabbits. *BMC complementary and alternative medicine,* 19**,** 1-7.

Shukla, A., Rasik, A. M. & Dhawan, B. N. 1999. Asiaticoside-induced elevation of antioxidant levels in healing wounds. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives,* 13**,** 50-54.

Speer, K., Tanner, N., Kölling-Speer, I., Rohleder, A., Zeippert, L., Beitlich, N. & Lichtenberg-Kraag, B. 2021. Cornflower honey as a model for authentication of unifloral honey using classical methods combined with plant-based marker substances such as lumichrome. *Journal of Agricultural and Food Chemistry,* 69**,** 11406-11416.

Su, J., Li, J., Liang, J., Zhang, K. & Li, J. 2021. Hydrogel preparation methods and biomaterials for wound dressing. *Life,* 11**,** 1016.

Tripathi, G., Mishra, S., Upadhyay, P., Purohit, S. & Dubey, G. 2015. Ethnopharmacological importance of Centella asiatica with special reference to neuroprotective activity. *Asian Journal of Pharmacology and Toxicology,* 3**,** 49-53.

Ullah, F., Othman, M. B. H., Javed, F., Ahmad, Z. & Akil, H. M. 2015. Classification, processing and application of hydrogels: A review. *Materials Science and Engineering: C,* 57**,** 414-433.

Velasco-Hogan, A., Xu, J. & Meyers, M. A. 2018. Additive manufacturing as a method to design and optimize bioinspired structures. *Advanced Materials,* 30**,** 1800940.

Visavadia, B. G., Honeysett, J. & Danford, M. H. 2008. Manuka honey dressing: An effective treatment for chronic wound infections. *British Journal of Oral and Maxillofacial Surgery,* 46**,** 55-56.

Wang, Z., Qi, F., Luo, H., Xu, G. & Wang, D. 2022. Inflammatory microenvironment of skin wounds. *Frontiers in immunology,* 13**,** 789274.

Xiang, L. Y., Mohammed, M. A. P. & Baharuddin, A. S. 2016. Characterisation of microcrystalline cellulose from oil palm fibres for food applications. *Carbohydrate polymers,* 148**,** 11-20.

Yap, S. & Chin, N. 2021. Identification of distinctive properties of common Malaysian honeys. *Materials Today: Proceedings,* 42**,** 115-118.

Yiin, C. L., Ho, S., Yusup, S., Quitain, A. T., Chan, Y. H., Loy, A. C. M. & Gwee, Y. L. 2019. Recovery of cellulose fibers from oil palm empty fruit bunch for pulp and paper using green delignification approach. *Bioresource technology,* 290**,** 121797.

Yousaf, S., Hanif, M. A., Rehman, R., Azeem, M. W. & Racoti, A. 2020. Indian Pennywort. *Medicinal Plants of South Asia.* Elsevier.

Yuan, P. 2013. *Design, fabrication, and application of stimuli-responsive hydrogel actuators,* University of Illinois at Urbana-Champaign.

Yusof, N. N. M., Rahman, T. A. F. T. A., A'wani Abd Aziz, N., Hadizam, B. B. & Isleih, A. R. I. S. 2020. Systematic literature review on Centella asiatica. *Sains Insani,* 5**,** 135-141.