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# Gradient Gels: Exploring Diverse Starch Concentrations in Hydrogel Formulations

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*Abstract:* *Starch hydrogels can be used for both drug formulation and delivery; they have attracted a lot of interest in the pharmaceutical dispensing industry. Four pharmacy students were tasked with creating starch hydrogels in this study, with different concentrations (2%, 4%, 5%, and 10%) to see how concentration affected the hydrogels' chemical and physical characteristics. The goal of this study was to provide important new information about how to optimise starch hydrogel formulations for use in medicine. The students gained an understanding of how concentration affects properties like viscosity, mechanical strength, and transparency by methodically studying these important variables. Furthermore, the investigation examined the impact of environmental variables like pH and temperature on the stability and functionality of the starch hydrogels.*

Key Words: Hydrogels, Viscosity, Concentration, Starch

## Introduction

Because of their hydrophilic structure, a class of polymeric materials known as hydrogel products may hold a large amount of water in their three-dimensional networks. It is thought to be crucial to use these goods extensively in a variety of industrial and environmental application areas. It was to be expected that synthetic hydrogels, with their greater capacity for absorbing water, longer shelf life, and greater range of basic chemical resources, would eventually replace natural hydrogels. Hydrogels are characterised by their unique three-dimensional crosslinked polymer meshwork structure, which allows them to retain the network structure in its swelled state while absorbing large volumes of water into their interstices and continuing to bond it. Because polar hydrophilic moieties, such as OH, NH2, COOH, etc., are present throughout the polymer network as branched groups, hydrogels are able to demonstrate such behaviours. The

hydrophilicity of connected groups, swelling media, and crosslinked bonding strength all indicate the swelling character of hydrogels, which is responsible for their propensity to absorb water. (Ghorpade 2019) In the swelled condition, crosslinking helps to preserve the network structure and regulates water absorption. In addition to participating in secondary interactions with biological tissues, crosslinkers are essential. (Ghorpade 2019)

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Hydrogels are essential in biomedical applications because of their unique qualities, which include superabsorbancy, hydrophilicity, biodegradability, biocompatibility, viscoelasticity, softness, and fluffiness. In addition, hydrogels react to a variety of stimuli, including ionic strength, temperature, electric and magnetic fields, and biological substances. One important feature of hydrogels for wearable and portable electronics is their ability to heal themselves. The gadgets' capacity for damage control or self-healing makes them perfect for smart, lightweight electronics. (Dimatteo 2018)

## Classification of Hydrogel

Hydrogels are classified based on a variety of factors, including the materials (polymers) utilised, their source, the crosslinking method, their response to stimuli, and their ionic charge. The hydrogels' polymers are either natural, synthetic, or a combination of both. Numerous hydrogels, such as terpolymers, copolymers, block copolymers, and homopolymers, can be created by combining these polymers.

Hydrogels can be categorised in the following ways based on their chemical makeup and physical structure:

- Lacking crystalline structure.
- Semicrystalline: A sophisticated blend of crystalline and amorphous phases.
- Crystalline.

## Classification according to Cross-linking Type

Hydrogels can be divided into two categories based on the type of cross-link junction—physical or chemical. Chemically cross-linked networks have permanent junctions, but physical networks have transient junctions because of physical interactions such as ionic, hydrophobic, or hydrogen bonding, or polymer chain entanglements.

## Categorization according to Outward Appearance

The preparation phase polymerization process determines how hydrogels form as a matrix, film, or microsphere.

## Arrangement Based on Network Electrical Charge

Depending on whether or not their cross-linked chains are electrically charged, hydrogels can be divided into four classes:

- Neutral (nonionic).
- Ionic, which comes in cationic and anionic forms.
- Amphoteric electrolyte, or ampholytic electrolyte, having both basic and acidic groups in it.
- Zwitterionic (polybetaines), where each structural repeating unit has a combination of cationic and anionic groups.

## The Biodegradability States

- Hydrogels that degrade naturally: Hydrogels degrade naturally. Biodegradable polymers found in nature include chitosan, fibrin, and agar. Synthetic biodegradable polymers include poly (aldehyde guluronate), polyanhydrides, and poly (N-isopropyl acrylamide). (Hu 2018) (Mohamed 2012)
- Hydrogels that are not biodegradable: Methoxyl poly (ethylene glycol), 2-hydroxyl propyl methacrylate, 2-hydroxyl ethyl methacrylate, and other vinylated monomers or macromers.

## Categorization Based on the Composition of Polymers

- Homo-polymeric hydrogels: Any polymer network is made up of monomers, which are the fundamental structural constituents. Polymer networks made from a single species of monomer are called homo-polymeric hydrogels. The kind of monomer and the polymerization process employed during the process are responsible for the cross-linked skeleton of homopolymers.

- Co-polymeric hydrogels: Co-polymeric hydrogels are made up of two or more different monomer species with at least one hydrophilic component that are organised in a random, block, or alternating arrangement along the chain of the polymer network.
- Multi-polymer interpenetrating polymeric hydrogel (IPN): Multi-polymer interpenetrating polymeric hydrogel (IPN), which is composed of two distinct cross-linked synthetic or natural polymer components, is a significant type of hydrogels. Semi-IPN hydrogel is composed of two types of polymers: cross-linked and non-cross-linked.

## Hydrogel Makeup

Because they are non-toxic, hydrogels made of naturally occurring polymers are referred to as "natural hydrogels" and are widely available at low cost. Natural polymers fall into different categories based on the way their molecules are arranged. Their chemical structure places them in a number of classes: The polymers that are classified as:

- Biological polymers (DNA and nucleic acid)
- Polyamides (collagen),
- Polyphenols (lignin),
- Organic polyesters,
- Inorganic polyesters (polyphosphazene)

Synthetic hydrogels are composed of synthetic polymers that provide increased flexibility in adjusting the hydrogel's mechanical properties.

- Polycaprolactone Poly (vinyl pyrrolidone)
- Poly (lactic acid)
- Poly (ethylene glycol)
- Poly (vinyl alcohol) (PVA)

Because PEG can combine with proteins, peptides, and some other drugs, it is especially important. Moreover, it is biocompatible, biodegradable, and water soluble. (Iresha 2020)

## Features of Hydrogel

- To create hydrogels for biomedical applications, it is highly advantageous to use polymers, either natural or synthetic, that have hydrophilic pendant groups.
- These groups not only allow for ample water absorption but also aid in the interaction with biological tissues, such as mucous membranes and epithelial tissues.
- When hydrogels are fully swollen, they typically have a low interfacial angle with biological fluids, are soft, rubbery, and almost viscoelastic, which reduces the likelihood of an adverse immune reaction.
- Depending on the material's intended use, the mechanical properties are modifiable and adjustable. Heating the material can result in a gel with greater stiffness by raising or decreasing the degree of crosslinking. Different analyses must be conducted depending on the material because variations in mechanical properties are linked to a wide range of variables and causes.

## Swelling behavior of Hydrogel

- The swelling ratio, which is used to measure swelling, is the weight swelling ratio of swollen gel to dry gel. Crosslinking has an effect on the swelling ratio of hydrogel; structures with higher crosslinking have lower swelling ratios, and vice versa. Because of the hydrophilic and hydrophobic groups on the polymer chains, chemical structure also has a major impact on the swelling property. (Ganji 2010)
- Hydrogels with more hydrophilic groups swell more than those with hydrophobic

groups. Two more factors that affect hydrogel swelling are pH and temperature. pH-sensitive hydrogels swell due to the ionisation of hydrophilic groups with changes in pH. Ionisation results in electrostatic repulsion between like charges on the polymer and breaks the secondary bonding between polymer chains.

- Hydrogel is referred to as the glassy condition when it is dehydrated and as the rubbery state when it is swelled. The solvent molecules can locate spaces in the chains when the glassy or dry hydrogel comes into contact with the watery media. When enough water has entered the hydrogel matrix, the glassy state transforms into the rubbery state, also referred to as swelling. Through the process of diffusion, water can enter and exit the hydrogel matrix. (Ganji 2010)

## Material and Method

### Different Concentrations of Hydrogel

Keeping in view sterile environment and appropriate raw material four pharmacy students of 5th semester prepared different samples of hydrogel formulations having concentrations i.e. 2% ,4%, 5% ,10% to determine their properties including spreadability , stiffness/thickness , swelling capacity, mechanical strength, adhesive properties and porosity. (Marriott 2010)

The polymer used was selected as starch dissolved in universal solvent i.e. water. The temperature conditions of the room was maintained at 22 degrees. After preparing the sample of each concentration they were heated at approx 50-55 degrees so that they could attain a gel like consistency, then allowed to set at room temperature for about 24 hours. Next day results were observed.

## Starch being used as a Polymer in Hydrogel Preparation

Polysaccharides, or complex carbohydrates made up of linked glucose units, are what make up starch. It is present in structures such as grains, tubers, and roots and is the main molecule used by plants to store energy. Plants can use starch as a store of energy to transform it into sugars for metabolism later on. It is made up of two primary parts: branched chain amylopectin and linear chain amylose, which are both composed of glucose molecules. Because of its abundance, affordability, and versatility, starch is a key ingredient in many staple foods and is utilized extensively in a variety of sectors. (Ismail 2013)

## Advantages of Starch as a Polymer

There are several benefits of using starch as a polymer in hydrogels, which makes it an appealing option for a range of applications. The main reasons for selecting starch as our polymer are;

Biodegradability: The ability to biodegrade Plants naturally produce starch, which is a biodegradable polymer. Starch hydrogels can decompose into non-toxic components and are safe for the environment.

Low Cost and Plenty: Many different plant sources, including corn, potatoes, and cassava, are good sources of starch. It is an inexpensive resource for hydrogel manufacturing due to its abundance.

Renewable Resource: Since starch is derived from plants that can be regenerated via farming, it is a renewable resource. Synthetic polymers, on the other hand, might depend on non-renewable resources.

Biocompatibility: In general, starch is biocompatible, which means that living things can accept it. Because of this, starch-based hydrogels can be used in a variety of pharmacological and medical applications.

Ease of Modification: It is simple to modify starch to give it new characteristics including increased mechanical strength, regulated release, and stimulus sensitivity. Because of its adaptability to a variety of uses, it is flexible.

Water Absorption and Swelling Properties: Hydrogels based on starch frequently have good swelling and water absorption qualities. These characteristics make them appropriate for use in controlled medicine delivery, agriculture, and wound treatments.

Formulation Versatility: A variety of polymers and substances can be blended with starch to form customized hybrid hydrogels. This makes it possible to create a broad variety of formulations to satisfy certain needs.

Compatibility with Food and medicinal Industries: Starch is widely utilized in the food business, and because of their biocompatibility and safety, starch-based hydrogels are well suited for food packaging, food preservation, and medicinal applications. (Jiang 2011)

## Discussion

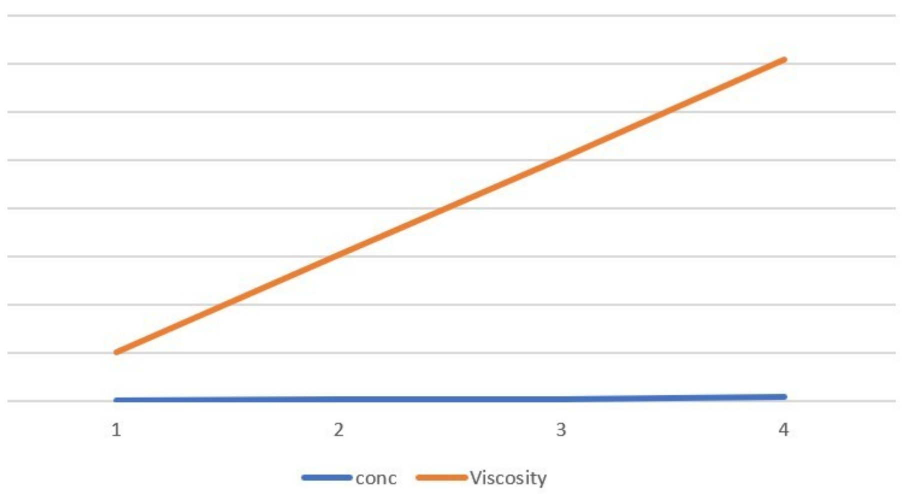
### Variables Affecting Hydro-Gels

Hydrogels, which are three-dimensional networks with a high-water holding capacity, are widely used in many industries, including medicine. Four pharmacy students have created **starch hydrogels** in this situation at varying concentrations of 2%, 4%, 5% and 10%. We will investigate the variables affecting these hydrogels, emphasizing their cross-linkages, pH effects and swelling characteristics.

### Viscosity and Concentration of Starch

The rheological characteristics of hydrogels are significantly influenced by the content of starch. In comparison to greater concentrations, the hydro-gel's viscosity and gel strength are probably going to be reduced at 2%. This is because starch molecules have a lower density, which leads to a looser network structure. The gel strength and viscosity rise in tandem with the concentration as it approaches 4%, 5%, and 10%. Stronger intermolecular connections result from a denser network generated by a higher concentration of starch molecules, which is the cause of this rise.

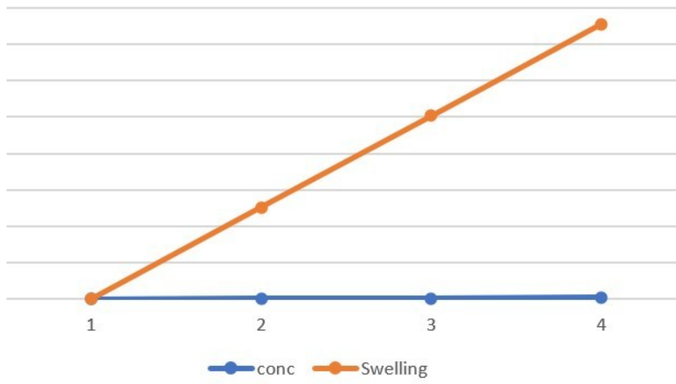
Figure 1




### Swelling Properties

One important characteristic of hydrogels that is affected by starch content is swelling. Faster swelling is made possible by the 2% hydro-gel's weaker network structure, though not as much as at higher concentrations. Since the network structure of the 4% hydrogel is more balanced, it shows modest swelling. When the concentration rises to 5% and 10%, the swelling gets more but happens more gradually. Higher concentrations of the closely spaced network impede the quick absorption of water, causing a gradual but noticeable swelling. (Ganji 2011)

Figure 2




## pH Effects

pH plays a crucial role in the stability and performance of starch hydrogels. A neutral to slightly acidic pH range is generally preferred. In the 2% hydrogel, maintaining a stable pH is important for its overall stability. As concentration increases, pH control becomes even more critical. The 4%, 5%, and 10% hydrogels would likely require a carefully controlled pH environment to ensure optimal performance. Deviations from the preferred pH range may lead to hydro-gel degradation, affecting its structural integrity and performance.

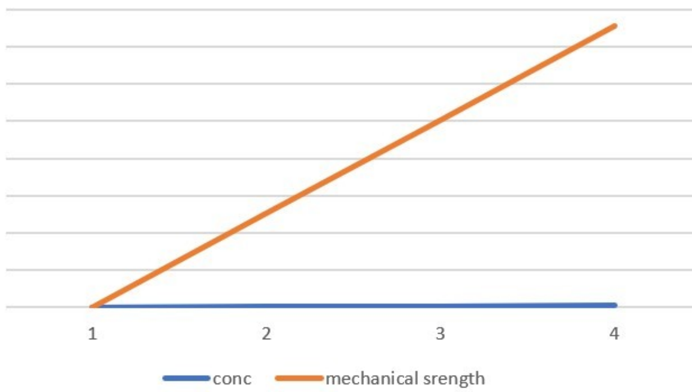
## Cross-linkages

A crucial component of the structure of hydrogels is the creation of cross-linkages. Less crosslinking results in a more open network structure in the 2% hydrogel. There might still be crosslinking agents, but only in smaller amounts. Cross-linkages grow dramatically as concentration rises to 4%, 5%, and 10%. An increase like this produces a more stiff and robust gel structure. With the maximum concentration, the 10% hydro-gel would have the densest crosslinkage network, making it a strong and stable hydro-gel.

## Molecular Interactions in Hydrogels

It is essential to comprehend the molecular interactions that occur within hydro-gels. Hydrogen bonds are formed by starch molecules, aiding in the gelation process. The comparatively sparse starch molecules at lower concentrations create fewer hydrogen bonds, which makes the hydro-gel softer and more pliable. The closer starch molecules are to one another, the stronger the hydrogen bonding between them and the more rigid the structure becomes.

Figure 3




## Impact of Cross-linking Agents

The hydro-gel properties are greatly impacted by the crosslinking agent selection and concentration. Genipin, epichlorohydrin, and glutaraldehyde are examples of common cross linking agents. Because of the reduced concentration in the 2% hydro-gel, the crosslinking agent may need to be lowered proportionately. In order to create a stable network, the 4%, 5%, and 10% hydro-gels would require larger crosslinking agent concentrations. The hydro-gel's mechanical strength and stability are largely dependent on the crosslinking process. (Lu 2009)

## Biocompatibility Considerations

In pharmaceutical applications, hydro-gels' biocompatibility is important. Since starch is an organic polysaccharide, it is usually regarded as biocompatible. Biocompatibility, however, can be impacted by crosslinking agents and concentration. While biological systems might be more receptive to lower doses, greater concentrations might provide difficulties. To achieve biocompatibility, the intended application and the biological environment must be carefully considered.

## Drug Release Properties

Drug delivery systems often employ hydrogels. The kinetics of drug release is influenced by the hydro-gel's starch concentration. Because of the more porous structure, lower doses may cause the drug to release more quickly, whilst higher concentrations result in a regulated and prolonged release. Drug release is further influenced by the crosslinking agent used; hydrogels with higher crosslinking tend to have slower release profiles. (Ghorpade 2019)

## Environmental Impact

When developing and employing hydrogels, it is essential to take the environment into account. Since starch is a renewable and biodegradable substance, it fits in nicely with eco-friendly methods. However, there may be environmental risks associated with the crosslinking agents utilized, particularly the synthetic ones. One line of inquiry for reducing environmental effect is the investigation of substitute, environmentally benign crosslinking agents.

## Result

Researchers explored various starch hydrogel concentrations—2%, 4%, 5%, and 10%. The lower concentrations (2% and 4%) exhibited improved transparency and reduced viscosity, making them promising for topical drug delivery, enhancing both aesthetics and patient compliance. In contrast, higher concentrations (5% and 10%) displayed increased mechanical strength and prolonged drug release, suggesting suitability for controlled-release formulations.

## Conclusion

The four pharmacy students worked together to prepare and investigate the effects of different concentrations (2%, 4%, 5%, and 10%) of starch hydrogels. This research has provided important insights into the composition and characteristics of these hydrogels. Lower concentrations of hydrogels (2% and 4%), however, showed improved transparency and decreased viscosity, indicating their possible use in topical drug delivery applications. Both aesthetic appeal and patient compliance may be enhanced by these concentrations. On the other hand, hydrogels at greater concentrations (5% and 10%) demonstrated enhanced mechanical strength and prolonged drug release profiles, suggesting their appropriateness for formulations with controlled release. This discovery has potential applications in the creation of pharmaceuticals with long-lasting therapeutic effects.

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