

## FORMULATION OF NOVEL WOUND HEALING HYDROGEL USING EXTRACTS OF PADINA TETRASTROMATICA AND DETERMINING ITS ANTIBACTERIAL ACTIVITY AGAINST WOUND PATHOGENS

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### ABSTRACT

Seaweeds are rich in polysaccharides and also possess antiviral, antibacterial, antifungal, antiprotozoal, and antifertility activities. The present study covers about the effective wound healing and prevention by Hydrogel prepared from extracts of seaweeds. The seaweed was extracted with solvents and the crude extract was separated using analytical thin-layer chromatography (TLC). The separated compounds and prepared hydrogel were tested for their potential antibacterial activity and anti-inflammatory activity against *Staphylococcus aureus* and *Klebsiella pneumoniae* bacteria. This study represented that the extracts of *Padina tetraströmatica* contain a variety of phytochemical compounds, which can effectively protect the body from inflammation and thus can be used as a potent source of natural protecting compounds.

Keywords: Hydrogel, Anti-inflammatory, TLC (Thin Layer Chromatography)

### 1.0 INTRODUCTION:

The seaweeds are collected from Rameshwaram, south coast of India. The alga *Padina tetraströmatica*, belongs to the order dictyotales of phaeophyta phylum, is found abundant in Indian coastal areas (Mohan et al., 2014). *P. tetraströmatica* was proved to be an upscale source of the foremost essential nutrients including vitamin B1, B2, B6, and minerals like copper, manganese, zinc, lead, etc. *Padina tetraströmatica* belongs to the *Dictyotaceae* family and is one among the foremost important marine brown seaweeds. Furthermore, Naqvi et al. 1(1981) investigated the biological activity of certain seaweeds from the Indian coast, including studies for antiviral, antibacterial, antifungal, antiprotozoal, and antifertility. A wound may be a relatively quick injury during which the skin is torn, cut, or punctured (an open wound), or a contusion is caused by blunt force trauma (a closed wound). It precisely refers to a pointy injury to the epidermis of the skin in pathology. Wounds that aren't healing should be investigated to seek out the causes; many microbiological agents could also be responsible. Diabetic foot

wounds that don't heal are one among the foremost severe complications of diabetes, posing an enormous medical, social, and economic burden that features a direct effect on patient quality of life(Chakraborty et al., 2009)..

This study covers about the effective wound healing and prevention by Hydrogel prepared from extracts of seaweeds. For effective wound healing it requires an appropriate material to stop the wound infection. The emergence of antibiotic resistance in pathogenic microbes is major crisis within the global health problems. The algal tests were tested for his or her antibacterial activity against multidrug resistant isolates of bacteria. during this study multidrug resistant of three bacteria are used against wound pathogens. The deep wound may damage the integrity of skin and damage the tissues , it's essential to require care the injuries properly because it's going to cause severe problems which just in case not treated(Napeng et.al.,2019). Hydrogels are cross-linked polymers which will be natural or synthetic and are utilized in variety of biomedical fields. it's made from an insoluble polymer matrix with a water content of about 96 percent.

These hydrogels will donate water to the wound site, aiding within the preservation of a moist atmosphere that aids wound healing .Many scientists are now working towards Hydrogels within the areas of agriculture, food industry, tissue engineering ,drug delivery and as regenerative medicine. Some sorts of hydrogels have inherent antibacterial activity. Recently Hydrogels are used due to their effectiveness and moist healing environment. Compared to other wound dressings Hydrogels are biodegradable, biocompatible and have low immunogenicity and straightforward usage. it's mainly wont to prevent and cure bacterial infections of wounds like burns, un healing wounds in diabetic patients ,tissue regeneration. There are various wound dressings to heal the injuries and to enhance health conditions but Hydrogels have unique compatibility that heal the injuries in moist environment, immediate pain relieving ,improved tissue repair and barrier against bacteria, oxygen permeability.

According to world health organization(WHO) the worldwide death rate is second place for the communicable disease . Hydrogels have increasing chemical, physical and biological properties compared to other dressings and even have a 3D cross linked polymer which may absorb and retain great deal of water. during this TIC is employed to isolate and purify the pigments from *Padina tetrastrum* seaweed. This include extraction of seaweeds with optimized low polarity solvent mixtures, isolation of crude extract using analytical thin layer chromatography(TLC),biological screening of the extract for its antimicrobial activities by

using TLC bio-autography. The hydrogel is ready by using seaweed extracts against multidrug pathogens like staphylococcus aureus, E.coli and klebsula pneumonia.(satarupa roy et.al.,2016).

## **2.0 MATERIALS AND METHODS:**

### **2.1 Collection of *Padina tetrastromatica* (Seaweed) and Authentication**

*Padina tetrastromatica* was collected from a shores of Rameshwaram, TamilNadu. It was authenticated by Dr. M.U. Sharief. Scientist 'E', Botanical Survey of India Southern Regional Centre, Coimbatore.

### **2.2 Extraction of bioactive compounds using Soxhlet apparatus**

*Padina tetrastromatica* was dried under room temperature and finely grounded to powder. Powders of *Padina tetrastromatica* was placed in a porous bag or "thimble" made from a strong filter paper or cellulose, which is placed, is in thimble chamber of the Soxhlet apparatus. Extraction solvent (methanol) is heated in the bottom flask, vaporizes into the sample thimble, and condenses in the condenser and drip back. When the liquid content reaches the siphon arm, the liquid contents is emptied into the bottom flask again and the process is continued. For the study, infusion method of Soxhlet Extraction had been adopted. The dried powder was filled in the thimble and placed in the soxhlet extractor. The extractor had been filled with solvent solution of methanol and the temperature of 60°C was set and left for 6hours. The extracts were collected and the solvents were evaporated. The dried extracts were collected and stored in sterile containers.

### **2.3 Phytochemical screening**

The methanolic extracts were subjected to qualitative phytochemical analysis.

#### **1. Alkaloids**

To 3 ml test solution, a few drops of dilute iodine solution were added. Blue colour indicates the presence of alkaloids.

#### **2. Flavonoids**

Alkaline reagent test was performed for checking the presence of flavonoids. The crude powder was treated with a few drops of diluted sodium hydroxide (NaOH) separately. Formation of intense yellow color which turned colorless on addition of a few drops of diluted HCl indicated the presence of flavonoids.

### **3. Tannins**

10 ml of bromine water was added to the 0.5 g aqueous extract. Decoloration of bromine water showed the presence of tannins.

### **4. Terpenoids**

Chloroform extract of the crude powder was treated with concentrated sulphuric acid (H<sub>2</sub>SO<sub>4</sub>). Appearance of reddish brown ring indicated the presence of terpenoids.<sup>13</sup>

### **5. Steroids**

Liebermann-Burchard reaction was performed for checking the presence of steroids. A chloroformic solution of the crude powder was treated with few drops of concentrated H<sub>2</sub>SO<sub>4</sub> were added down the sides of the test tube. A blue green ring indicated the presence of steroids.

### **6. Saponins**

The presence of saponins was determined by Frothing test. The crude powder was vigorously shaken with distilled water and was allowed to stand for 10 min and classified for saponin content as follows: no froth indicates absence of saponins and stable froth of more than 1.5 cm indicated the presence of saponins.<sup>18</sup>

### **7. Cardiac glycosides**

Keller-kiliani test was performed for checking the presence of cardiac glycosides. The crude powder was treated with 1.0 ml mixture of 5% FeCl<sub>3</sub> and glacial acetic acid (1:99 v v-1). To this solution, a few drops of concentrated H<sub>2</sub>SO<sub>4</sub> were added. Appearance of greenish blue colour within few minutes indicated the presence of cardiac glycosides

### **8. Phenol**

0.5 ml of FeCl<sub>3</sub> (w/v) solution was added in 2 ml of test solution, formation of an intense color indicates the presence of phenols.

### **9. Quinones**

Extracts was treated with concentrated HCl appearance of green colouration indicates presence of Quinone.

### **10. Test for Fixed oil (Filter paper test)**

A small quantity of the extracts was pressed between 2 two filter papers. Appearance of oil strain on the paper indicates the presence of fixed oils and fat.

## **2.4 Preparation of wound healing gels**

Wound dressing gels was developed by the method described by Natarajan *et al.*, 2018. Poly vinyl alcohol (2%) is mixed with the distilled water and stirred under room temperature. Under stirring conditions 2% of seaweed extracts were added drop wise. 2% citric acid is added to the solution and stirred for 30mins. The films were poured in a plastic petri dish and kept undisturbed overnight. Later the gels were used for further analysis.

## **2.5 TLC and anti bacterial activity against bioactive compounds**

The extracts were taken in a capillary tube and it was spotted in preparative TLC plates coated with silica gel G. The plates were developed in TLC chamber previously saturated with different solvent systems. The different spots developed in each solvent system were identified by means of detecting agent and the R<sub>f</sub> value are correspondingly calculated 1,4.(Mobile phase : Butanol: Methanol: Water – 5:3:2).

## **2.6 Antibacterial activity of the seaweed extracts and wound healing gel against wound causing pathogens**

The antibacterial efficacy of the seaweed extracts and wound healing gel was evaluated against the two major wound pathogen *Staphylococcus aureus* and *Klebsiella pneumoniae* by well diffusion method. Nutrient Agar was prepared and sterilized, and poured into plates. (Nutrient agar Composition (for 100ml): Peptone: 0.5g; Yeast extract: 0.5g, Beef extract: 0.3g, Sodium chloride: 0.5g, Agar 1.5 g; Total pH: 7.0 ± 0.2). Overnight cultures of test pathogens were cultured and 0.1% of culture solution of each test organisms was streaked throughout the petri plate with the sterile cotton swab by roating the plate at 60° angle for each streaking. 6mm well borer was used to bore wells on the agar surface of each NA plates. About 100µl of the samples were loaded into the well and the plates were incubated in an incubator at 37°C for 48h. The antibacterial activity was determined in terms of inhibitory zones around the wells loaded with natural dyes in all the Nutrient Agar plates containing test pathogens. The obtained clear zones were observed and measured in millimetre (mm).

## **2.7 Anti-inflammatory activity of the extract**

The anti-inflammatory activity of seaweed extract was studied by using inhibition of albumin denaturation technique which was studied according to Mizushima et al and Sakat et al followed with minor modifications. The reaction mixture was consists of test extracts and 1% aqueous solution of bovine albumin fraction, pH of the reaction mixture was adjusted using small amount of 1N HCl. The sample extracts were incubated at 37 °C for 20 min and then heated to 51 °C for 20 min, after cooling the samples the turbidity was measured at 660nm.( UVVisible Spectrophotometer Model 371, Elico India Ltd) The experiment was performed in triplicate. The Percentage inhibition of protein denaturation was calculated as follows:

$$\text{Percentage inhibition} = (\text{Abs Control} - \text{Abs Sample}) \times 100 / \text{Abs control}$$

### 2.7.1 Anti proteinase activity

The test was performed according to the modified method of Oyedepo *et al.*, 1995 and Sakat *et al.*, 2010. The reaction mixture (2 ml) was containing 0.06 mg trypsin, 1 ml 20 mM Tris HCl buffer (pH 7.4) and 1ml test sample of different concentrations (100 – 500 µg/ml). The mixture was incubated at 37°C for 5 min and then 1 ml of 0.8% (w/v) casein was added. The mixture was incubated for an additional 20 min. 2 ml of 70% perchloric acid was added to arrest the reaction. Cloudy suspension was centrifuged and the absorbance of the supernatant was read at 210 nm against buffer as blank. The experiment was performed in triplicate. The percentage inhibition of proteinase inhibitory activity was calculated.

$$\text{Percentage inhibition} = (\text{Abs control} - \text{Abs sample}) \times 100 / \text{Abs control}$$

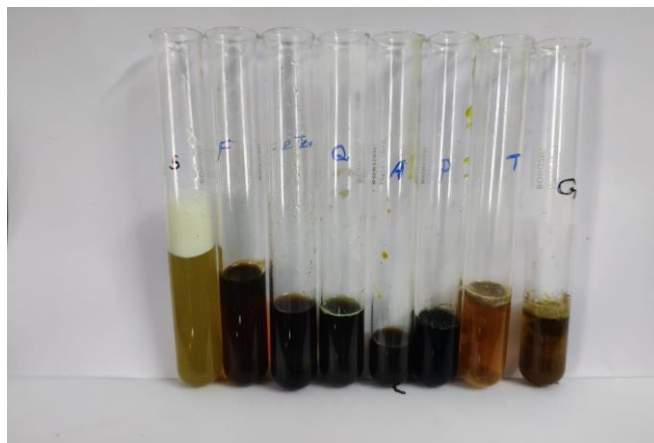
## 3.0 RESULT

### 3.1 Phytochemical screening

Preliminary phytochemical screening of Seaweed *Padina tetrastromatica* was carried out with aqueous extracts and the data was represented in table 1. The extract was made out by using soxhlet apparatus methods. The preliminary phytochemical studies revealed the presence of alkaloids, steroids, glycosides and flavonoids in aqueous extract. Some phyto constituents were observed in aqueous extract viz., steroids, glycosides and flavonoids. Further, some phyto-constituents like alkaloids, steroids, glycosides, flavonoids and tannins were shown in

aqueous extract. The resulting phytochemical analysis of *Piper nigrum* have shown in the Figure-1, Table.1.

**Figure-1: Phytochemical screening of seaweed extracts**



**Table-1: Phytochemical screening**

S. No	Phytochemicals	Observation
1	Alkaloids	-
2	Flavonoids	+
3	Saponins	+
4	Tannins	+
5	Steroids	-
6	Terpenoids	+
7	Phenol	+
8	Glycosides	-
9	Quinone	+
10	Oil	+

The presence and absence of the phytoconstituents in the seaweed *Padina tetrastrum* shown positive(+ present).

Preliminary phytochemical screening of seaweed *Padina tetrastromatica* clearly shows the presence of various phytoconstituents like flavonoids, terpenoids tannins, phenol, Quinone, oil, saponins .

### 3.2 TLC and Antibacterial activity of bioactive compounds

The seaweed *padina tetrastromatica* extracts were taken in a capillary tube and spotted in the preparative TLC plates with silica gel G. The plates were developed in TLC chamber which is saturated with solvent systems (mobile phase: Butanol: methanol :water -5:3:2). The spot expressed was seen under the uv light is shown in the figure 2.

**Figure -2 : TLC for extracts of seaweed *Padina tetrastromatica***



The antibacterial activity was performed for scrapped extracts from the TLC plates against the gram negative bacteria *klebsula pneumoniae* which is shown in the figure 3 and against one gram positive bacteria *Staphylococcus aureus* shown in figure 4.

**Figure -3 Antibacterial activity of *Klebsula pneumonia***





**Figure -4:Anti-bacterial activity against *Staphylococcus aureus*****Table-2:Anti-bacterial activity of bioactive compounds**

S. No	Sample	Inhibitory zones (mm)	
		<i>Staphylococcus aureus</i>	<i>Klebsiella pneumoniae</i>
1	20 $\mu$ g	-	-
2	40 $\mu$ g	12	13
3	60 $\mu$ g	15	14
4	Drug(ciproflaxin)	16	17

The above table shows at 20  $\mu$ g concentration the sample has no inhibitory zones against the bacteria *Staphylococcus aureus* and *Klebsiella pneumoniae*. The standard drug ciproflaxin shows 16mm and 17 mm, the 40  $\mu$ g concentration shows 12mm and 13mm, 60  $\mu$ g concentration of sample shows 15mm and 14 mm inhibitory zones respectively against the bacteria *Staphylococcus aureus* and *Klebsiella pneumoniae*.

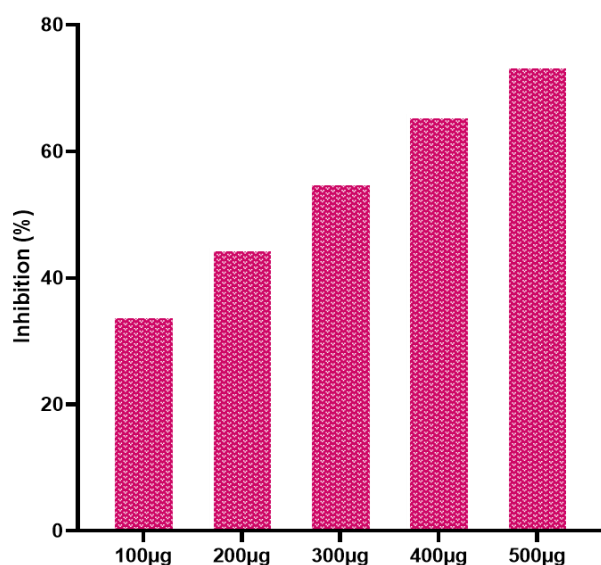
### 3.3 In-vitro Anti-inflammatory test

The anti-inflammatory activity of seaweed *Padina tetrastromatica* extract was studied by using inhibition of albumin denaturation technique which was studied according to Mizushima *et al* and Sakat *et al*. As part of the investigation on the mechanism of the anti-inflammatory activity, extracts were effective in inhibiting process. The Percentage inhibition of protein denaturation was calculated as follows:

$$\text{Percentage inhibition} = (\text{Abs Control} - \text{Abs Sample}) \times 100 / \text{Abs control}$$

**Table-3: Effect of seaweed extract on heat induced protein denaturation**

Concentration (µg)	Absorbance at 660nm	% inhibition of protein denaturation
Control	0.38	-
100	0.25	34.21
200	0.21	44.73
300	0.17	55.26
400	0.13	65.79
500	0.10	73.68

**FIGURE - 5: A graphical representation of anti inflammatory activity**

The above table and graph shows the seaweed *Padina tetrastromatica* extract at 100 to 500 µg it shows 34% to 73% inhibitory activity respectively, which is measured at 660nm.

### 3.3.1 Anti-proteinase action

The test was performed according to the modified method of Oyedepo *et al.*, 1995 and Sakat *et al.*, 2010. Cloudy suspension was centrifuged and the absorbance of the supernatant was read at 210 nm against buffer as blank. The experiment was performed in triplicate. The percentage inhibition of proteinase inhibitory activity was calculated.

$$\text{Percentage inhibition} = (\text{Abs control} - \text{Abs sample}) \times 100 / \text{Abs control}$$

**Table-4: Effect of seaweed extract proteinase inhibition**

Concentration (µg)	Absorbance at 660nm	% inhibition of proteinase
Control	0.38	-
100	0.31	18.42
200	0.29	23.68
300	0.26	31.57
400	0.24	36.84
500	0.21	44.73

### 3.4 In-vitro Anti-bacterial activity

The antibacterial efficacy of the seaweed *Padina tetrastrum* extracts and wound healing gel was evaluated against the two major wound pathogen *Staphylococcus aureus* and *Klebsiella pneumoniae* by well diffusion method. About 100µl of the samples were loaded into the well and the plates were incubated in an incubator at 37°C for 48h. The antibacterial activity was determined in terms of inhibitory zones around the wells loaded with natural dyes in all the Nutrient Agar plates containing test pathogens. The obtained clear zones were observed and measured in millimetre (mm).

**Figure-6: Antibacterial activity of seaweed extract and wound healing gel against *S. aureus***



**Figure-7: Antibacterial activity of seaweed extract and wound healing gel against *K. pneumoniae***



**Table-5: Antibacterial activity of seaweed extract and wound healing gel**

S. No	Sample	Inhibitory zones (mm)	
		<i>Staphylococcus aureus</i>	<i>Klebsiella pneumoniae</i>
1	Methanol	-	-
2	Drug (Ciprofloxacin)	16	13
3	Extract	10	8
4	Gel	9	10

The above table shows plain methanol has no inhibitory zones against the bacteria *Staphylococcus aureus* and *Klebsiella pneumoniae*. The standard drug Ciproflaxin shows 16mm and 13 mm, the *Padina tetrastromatica* extract shows 10mm and 8mm, the hydrogel shows 9mm and 10 mm inhibitory zones respectively against the bacteria *Staphylococcus aureus* and *Klebsiella pneumoniae*.

#### 4.0 DISCUSSION:

Hydrogels have existed for more than half century, providing one of the earliest records of crosslinked hydroxyethyl methacrylate (HEMA) hydrogels. Today, hydrogels still fascinate material scientists and biomedical researchers and great strides have been made in terms of their formulations and applications. As a class of material, hydrogels are unique, they consist of a self-supporting, water swollen three-dimensional (3D) viscoelastic network which permits the diffusion and attachment of molecules and cells. However, hydrogels have recently drawn great attention for use in a wide variety of biomedical applications such as cell therapeutics, wound healing, cartilage/bone regeneration and the sustained release of drugs. This is due to their biocompatibility and the similarity of their physical properties to natural tissue ( **Chirani N, Yahia LH, Gritsch L, et al**). In the previous work of Antonio francesko et.al. 2017 has reported that hydrogels are composed in a large extent of water and due to their non adhesiveness, it is used in wound dressing market and it provides a moisture environment for healing which is comfortable to the patient. The Hydrogel using are increases due to resemblance to dermal tissue and ability to induce partial skin regeneration. The innovation in advanced wound care is further directed to the development of so called active dressings, where hydrogels are combined with components that enhance the primary purpose of providing a beneficial environment for wound healing.

As we are discussed above there are numerous properties in seaweed *Padina tetrastromatica* which possess anti-viral, anti-bacterial, anti-inflammatory, anti-oncogenic, anti-tumor activity and also anti potent HIV agent. The hydrogels are having great unique properties and are prepared from many seaweeds and also as biofilms etc. The hydrogel prepared by using the extract of seaweed *Padina tetrastromatica* is first time. In this study we explore antibacterial activity of seaweed extract and wound hydrogel. Significant anti-bacterial activity is due to the presence of several bioactive compounds in the *padina* extract.

## 5.0. CONCLUSION:

Bacterial infection is a major reason for delayed wound healing, the development of drug resistant makes search for new anti bacterial compound. The phytochemical analysis have shown that the plant extracts possess flavonoids, tannins and steroids were present in aqueous extracts. In this study we explore antibacterial activity of *Padina tetrastromatica* extract and developed wound hydrogel. Both *Padina tetrastromatica* extract and gel shows better bacterial activity against major wound causing pathogens *Klebsula pneumoniae* and *Staphylococcus aureus*.

In the study represented that the extracts of *Padina tetrastromatica* contain a variety of phytochemical compounds, which can effectively protect the body from inflammation and thus can be used as a potent source of natural protecting compounds. In future, studies could be conducted to establish the anti inflammation mechanism of aqueous extract of sample. With all these results, we can conclude that *Padina tetrastromatica* can be used as a source of safe and natural protecting compounds against inflammation and can be used for treatment of prevention of wound infections. Significant anti bacterial is due to the presence of several bioactive compounds in this *padina tetrastromatica* extract. Moreover *Padina tetrastromatica* extracts also showed anti proteinase activity .Since *padina tetrastromatica* have more biological activities this will promote wound healing.

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GC-MS ANALYSIS, ANTIOXIDANT AND ANTIBACTERIAL ACTIVITY OF THE BROWN ALGAE, *PADINA TETRASTROMATICA* M. Uma Maheswari , A. Reena and C. Sivaraj Department of Microbiology , Mohamed Sathak College of Arts and Science, Chennai - 600119, Tamil Nadu, India. Armats Biotek Training and Research Institute  
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