

## Unlocking the pharmacological potential of earthworms: Proteins, enzymes, and immunoprotective agents

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### Abstract

For millennia, people have understood that earthworms had medicinal benefits. The history of traditional Southeast Asian medicine (China, Japan, Vietnam) makes this clear. Earthworms provide proteins, peptides, enzymes, and other physiologically active materials. As a result, a variety of ailments have been treated using extracts made from earthworm tissue. Similar to other intricate invertebrates, earthworms have many leukocyte subtypes that produce and release a range of chemicals that are immunoprotective. Phagocytosis, encapsulation, agglutination, opsonization, clotting, and lysis of foreign substances are all processes carried out by the immune-protective system. The two main leukocytes, small and big coelomocytes, mediate the lytic responses against several targets. Over the last ten years, scientists have identified and investigated many of the lytic, immune-stimulating, and clot-dissolving chemicals found in earthworms in lab and clinical settings. Scientists have focused their research on chemicals that dissolve clots. Researchers have isolated and examined fibrinolytic enzymes from various earthworm species, including *Lumbricus rubellus* and *Eisenia fetida*. These enzymes are considered to be strong and harmless. Clinical trials have validated its preventative and therapeutic benefits for thrombosis-related diseases. However, a number of investigations have shown that certain macromolecules found in earthworm extracts have a range of properties, including anticancer, antibacterial, anti-inflammatory, and antioxidant properties. Several of these activities include using an earthworm preparation for wound healing.

**Keywords:** *L. rubellus*, *E. fetida*, immunoprotective, leukocyte, phagocytosis

### Introduction

#### The Therapeutic Uses of Earthworms

We divided the medications into two categories based on the derived chemicals: plant-based medicine and animal-based medicine. We used animal components, particularly fluids and excrements, or non-animal materials like nests and cocoons. Similarly, researchers used plant components such as roots, stems, leaves, flowers, fruits, and nuts to make plant-based medication. Thus far, the World Health Organization has approved 252 essential chemicals for use, with 11.1% originating from plants and 8.7% from animals (Costa-Neto, 2005). This study investigates the various applications of earthworms in different countries for the treatment of various illnesses, including live, dried, powdered, paste, and extracts (Fig 1).

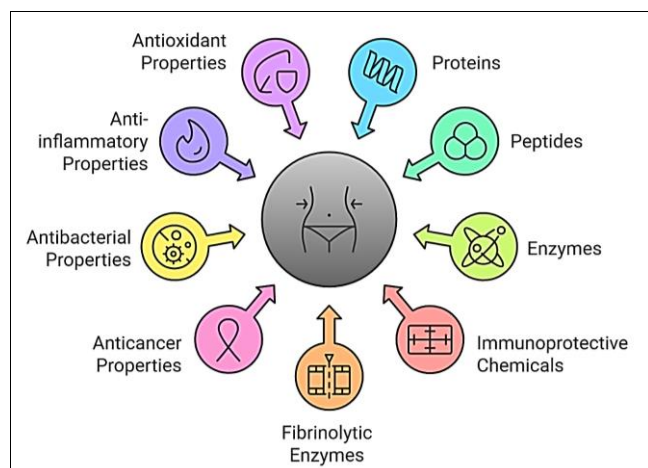


Fig 1: Medicinal properties of earthworms

People and animals in China, Japan, New Zealand, New Guinea, and Africa utilize earthworms as food due to their high protein content. People also consume or administer earthworms topically to treat ailments and disorders such as pimples, fever, smallpox, jaundice, and bladder stone removal. People apply earthworm ashes to their heads to promote hair growth or use them as teeth powder. Researchers have reported the following effects of earthworms or their extracts: rheumatism, impotence, lactation promotion, bronchial dilatation, pregnancy testing, and substance carcinogenicity testing.

For thousands of years, people have used earthworms and their derivatives for their medicinal properties. Indigenous medicinal expertise from around the world, but especially from Asia, which includes Korea, Vietnam, China, India, and Myanmar, has been critical in finding, isolating, and using physiologically active substances from earthworms. Since earthworms are soil-dwelling organisms, they are high in nutrients. China has been studying the therapeutic properties of earthworms for about 4,000 years. An allergy research group created "earthworm," a medication that is effective for treating gastrointestinal disorders, especially those involving inflammation of the gastrointestinal system. Additionally, people use earthworm tonic to balance the parasympathetic and sympathetic pathways of the central nervous system. It is customary in Korea to have "earthworm soup" before bed, which improves overall health and wards off numerous illnesses. The Vietnamese used earthworms as a "miracle medicine that could save lives in 60 minutes" for serious burns, hemorrhagic fevers, blood infections, and strokes. Strong, salty, "fishy," or both flavors of earthworms can cause nausea and vomiting in sensitive people. Pregnant or nursing women should avoid

consuming earthworm powder or combining it with other herbs or citrus fruits to prevent nausea and vomiting. We have not yet discovered any interactions between earthworms and drugs. Tribal peoples use earthworm treatment in addition to other herbal cures or nutritional supplements. Several studies on earthworms have shown that they can lower fevers, ease muscle spasms, remove toxins, help with water retention, lower blood pressure, fight allergies and asthma, kill germs, fight cancer and other infections, and reduce inflammation.

Apart from their multifunctional roles as makers of compost, proteins, land reclamation, and environmental cleansers, earthworms have long been used in medicine to treat a range of human ailments. People have used earthworm pastes or extracts to cure a variety of conditions, such as jaundice, hypertension, facial paralysis, impotence, chronic boils, piles, sore throats, hernias, chronic coughs, and bronchitis. Traditional Chinese medicine attributes antipyretic, antispasmodic, and diuretic properties to earthworms. Traditional medicine uses them to cure smallpox, pyorrhea, and to support nursing mothers. There is a suggestion that earthworms' antipyretic function is due to the presence of archiclonic acid inside their bodies. Historical evidence supports the effectiveness of earthworms in the treatment of rheumatism (Julka, 2008). China, North and South Korea, Thailand, and the Philippines use earthworms medicinally and clinically.

For at least 2,300 years, China has used earthworms for traditional medicine. Nitrogenous compounds derived from earthworms can expand human airways and lungs, and they can also serve as an anti-histamine for asthma treatment. Ancient Chinese medicine texts like "Qianjinfang," "Danxifang," "Jixaofang," and Bencagangmu used Dilong, the Chinese medicinal name for earthworm, as an antipyretic and anesthetic, for detoxification, to treat hypertension, to hasten parturition, and to treat a variety of common ailments like arthritis, itching, burns, carbuncles, erysipeias, and inflammation. Advances in contemporary science have led to the identification of certain earthworm active chemicals, such as terrestrolumbrolysin and linnbritin. Recently, scientists isolated an enzyme from earthworms that may dissolve blood thrombi in laboratory settings. Most likely, the pharmaceutical industry will turn this into an oral medication to prevent cardiovascular disease (Wang, pers.com).

### Earthworms' Pharmaceutical Composition

Earthworms contain substances such as hypoxanthine, lumbricin, terrestrolumbrolysin, and lumbrifibrin, as well as other purines, pyridines, choline, and guanidine. Earthworm fat is rich in compounds such as octadecanoic acids, palmitic acids, branched fatty acids, linear and carbon fatty acids, phosphatides, and cholesterol. It also contains high-chain unsaturated fatty acids. The yellow chlorogenous cells and organs of *Lumbricus terrestris* contain enormous amounts of alkaline amino acids, proteins, carbohydrates, lipids, and pigments. The yellow pigments could originate from riboflavin or its analogs.

Microelements including Zn (59.1 g/g), Cu (25.4 g/g), Fe (1735.5 g/g), Cr 10.93 g/g, Mo 0.25 g/g, Ca 1019.2 g/g, and Mn 1143 g/g are abundant in the tissues of the *Pheretima* species (Zhao, 1988). Crude protein (57.96%), crude fat (6.53%), crude ash (21.09%), crude fiber (0.36%), and N

extract (14.06%) make up *Allolobophora caliginosa*. These *Eisenia fetida* samples include crude protein (64.61%), crude fat (12.29%), crude ash (10.16%), crude fiber (0.27%), and N extract (12.67%). The ones that are a part of *Rosea* contain 63.71% crude protein, 12.29% crude fat, 10.66% crude ash, 0.21% crude fiber, and 12.67% N extract. *Lumbricus terrestris* possesses extremely low levels of glucose (0.01-0.05 µg/ml) in its blood and bodily fluids but high levels of lipids (35.14% neutral fat, 41.74% glucolipid, and 23.12% phosphatide). The principal components of the neutral fat are lauric acid, oleate, myristic acid, and decanoic acid. Decanoic acid and a few other short-chain fatty acids make up the fatty acids in glucolipids. The bulk of the fatty acids in the phosphate are behenic, oleate, decanoic, and linoleate acids. The proportion of unsaturated fatty acids is higher than that of saccharides and neutral fatty acids. A P-peptide complex is present in the gut wall of *Lumbricus terrestris*.

*Lumbricus terrestris* yellow chlorogenous cells and organs contain a variety of active enzymes. These include catalase, peroxidase, dismutase, β-D-glucosyl enzyme, alkaline phosphatase, esterase, S-amino-γ-ketoglutaric dehydrogenase, and porphyrin synthetase. *Eisenia* species' bodily fluids contain at least eighteen proteins with molecular weights ranging from 1,000 to 95,000 Da.

A protein that has the ability to hydrolyze collagen is present in the dormant species of *Allolobophora caliginosa*. Researchers from China, Korea, and Japan have identified and isolated fibrin-soluble enzymes from the digestive tracts and bodily fluids of earthworms. Researchers have created these enzymes as novel medications to treat myocardial infarctions and cerebral thromboses. Identified and isolated a type of acidic antibacterial peptide known as tetradecapeptide. Sun used this peptide to create a nutrient-rich, disease-resistant earthworm preparation suitable for both plant and animal production. Additionally, the body tissue of earthworms contains an enzyme that, under certain circumstances, may disintegrate the worms after they have died.

## Earthworms' pharmacological and clinical roles

### 1. The Nervous System's Impact

Zhang's work from the 1950s suggests that earthworms may reduce blood pressure. When Xu *et al.* administered macerated earthworm extracts in hot water and ethanol solution to anesthetized dogs, they saw a significant decrease in blood pressure. In an experiment, Xu poured medication into an excised rabbit heart. The results showed that a dose of 0.001% earthworm macerated extracts combined in hot water and ethanol solution may enhance the heartbeat, but it would decrease at a level of 0.05–1%. The rabbit's cardiac beat gradually decreased until it reached a dose of 0.1 g/kg body weight. Heart rhythm and ECG rates did not change at a dose that was 15–17 times greater than the dog's clinical enema. Xu observed that cardiac restrictions alone could not explain the depressed processes in earthworms. Using an ion-exchange column, Wang isolated an effective depressive component B1 from earthworm tissues. Researchers discovered that earthworms exhibit anti-excitation properties akin to those of coffee, and they could potentially reduce a specific type of hypertension by notably stimulating the sciatic nerves in the central forward direction. Wang concluded that the central nerve of

the upper spinal cord, which reflexes specific inner receptors directly and causes certain internal blood vessels to swell, is the fundamental cause of depressions. Kuang (1984) proposed that a 100% extract of earthworm tissues could prevent brain death due to insufficient blood flow by

enhancing the metabolism of 5-hydroxy tryptamine (5-HT) and dopamine (DA). These are the monoamines that facilitate communication between spinal cord and brain nerve cells (Table 1).

**Table 1:** Medicinal uses of earthworms

Medicinal Use	Description	Earthworm Species	Active Compounds	Application
Wound healing	Earthworm extracts accelerate the wound healing process.	<i>Lumbricus rubellus</i>	Lumbrofebrin, hydrolytic enzymes	Used in traditional medicine for topical application on wounds.
Antibacterial activity	Exhibits antimicrobial properties against gram-positive and gram-negative bacteria.	<i>Perionyx excavatus</i> , <i>Eisenia fetida</i>	Fetidin, lysenin	Used to treat bacterial infections or as a topical application for infections.
Anti-inflammatory effects	Earthworm extracts reduce inflammation and edema.	<i>Lumbricus rubellus</i>	Lumbrokinase, protease inhibitors	Helps in treating inflammatory conditions like arthritis.
Antioxidant properties	Earthworm extracts neutralize free radicals.	<i>Eisenia fetida</i>	Phenolic compounds, proteolytic enzymes	Used in formulations for boosting overall health and reducing oxidative stress.
Anticoagulant and fibrinolytic	Helps in breaking down blood clots and prevents coagulation.	<i>Lumbricus rubellus</i> , <i>Eudrilus eugeniae</i>	Lumbrokinase, fibrinolytic enzymes	Potential in treating thrombosis and related cardiovascular diseases.
Immune modulation	Earthworm extracts stimulate the immune system and improve immune response.	<i>Perionyx excavatus</i>	Polysaccharides, glycoproteins	Used in immune-enhancing therapies.
Anticancer activity	Earthworm extracts exhibit antitumor effects.	<i>Lumbricus rubellus</i>	Proteins, polysaccharides	Used in traditional cancer therapies; research ongoing for modern use.
Anti-ulcer activity	Earthworm extracts help prevent or heal gastric ulcers.	<i>Lumbricus rubellus</i>	Proteolytic enzymes	Used in traditional remedies for gastric issues.
Pain relief	Earthworm-based ointments and extracts are used to relieve pain.	<i>Lumbricus rubellus</i> , <i>Eisenia fetida</i>	Proteins, lumbrokinase	Applied topically or orally for pain management, especially joint pain.
Skin disorders treatment	Used in traditional remedies for treating eczema, psoriasis, and other skin ailments.	<i>Lumbricus rubellus</i>	Proteins, hydrolytic enzymes	Applied in topical formulations for treating skin issues.
Antidiabetic effects	Earthworm extracts may help in lowering blood glucose levels.	<i>Eisenia fetida</i> , <i>Lumbricus rubellus</i>	Polysaccharides, proteins	Potential use in managing diabetes; research ongoing.
Anti-fatigue properties	Helps in reducing fatigue and improving overall energy levels.	<i>Eudrilus eugeniae</i>	Amino acids, proteins	Used in traditional remedies for combating fatigue.
Liver protection	Earthworm extracts exhibit hepatoprotective properties, aiding liver detoxification.	<i>Lumbricus rubellus</i>	Enzymes, polysaccharides	Used to support liver health and detoxification.
Antihypertensive effects	Earthworm extracts may assist in lowering blood pressure.	<i>Eisenia fetida</i> , <i>Perionyx excavatus</i>	Peptides, proteins	Potential use in managing hypertension.
Antiallergic properties	Earthworm extracts may help in alleviating allergic reactions.	<i>Lumbricus rubellus</i>	Proteins, polysaccharides	Used in traditional treatments for allergies.
Neuroprotective effects	Extracts have potential neuroprotective properties that might protect against neurodegenerative diseases.	<i>Lumbricus rubellus</i> , <i>Eisenia fetida</i>	Neuroprotective peptides, proteins	Research ongoing for potential use in neurodegenerative disease management.
Digestive health support	Earthworm extracts promote digestive health and gut function.	<i>Eisenia fetida</i> , <i>Perionyx excavatus</i>	Enzymes, proteins	Used to enhance digestive health and treat gastrointestinal issues.
Anti-aging effects	Earthworm extracts may help reduce signs of aging by improving skin elasticity and reducing wrinkles.	<i>Lumbricus rubellus</i>	Collagen, proteins	Applied in anti-aging skin care products.
Anti-parasitic activity	Earthworm extracts exhibit activity against certain parasitic infections.	<i>Lumbricus rubellus</i> , <i>Eisenia fetida</i>	Bioactive compounds	Potential use in treating parasitic infections.
Anti-cholesterol effects	Earthworm extracts help lower cholesterol levels and improve lipid profiles.	<i>Eudrilus eugeniae</i>	Proteins, polysaccharides	Used in traditional remedies to manage cholesterol levels.
Enhancement of mental clarity	Earthworm extracts might aid in improving cognitive functions and mental clarity.	<i>Lumbricus rubellus</i> , <i>Eisenia fetida</i>	Neuroactive compounds, proteins	Used in traditional medicine for cognitive health.

## 2. Earthworms' Impact on the Blood System

Rao suggested that an enzyme present in earthworms' bodily fluids could potentially break down fibrin thrombosis. In earthworm extracts, scientist Li compared six thrombosis indicators: viscosity angle, pro-thrombosis development time, thrombus formation time, fibrin thrombus dissolving time, thrombus length, and dry weight. The goal was to find ways to stop blood clots from forming. Cheng looked into how different earthworm extracts affected the breakdown rates of a rabbit thrombus made from human pure fibrin coagulum, blood plasma with platelets, and whole blood coagulum. The findings demonstrated the considerable benefits of earthworm protein extracts and crude extracts on the dissolution of different types of thrombi in humans and rabbits. Cheng determined the thrombus-dissolving function by directly hydrolyzing fibrin.

## 3. Earthworms' Impact on the Cardiovascular System

This was shown by Shen in 1982: giving earthworms a dose of 0.5 grams per milliliter stopped arrhythmia in models made with barium chloride, ectisine, and chloroform-adrenaline, in that order. Additionally, the agent's K<sup>+</sup> content does not cause brief conduction pauses between the ventricle and atrium.

## 4. Earthworms' Impact on the Respiratory System

In the 1930s, earthworms easily became an effective asthma-prevention ingredient. Studies on rabbit lungs revealed that this ingredient induced bronchiectasis, potentially preventing asthma due to histamine and pilocarpine. The experimental animals received venous injections of this component.

## 5. Effect on Smooth Uterus Muscles

Xu isolated a type of material that may cause the smooth muscle in the uterus to contract. According to the experiment's findings, this chemical significantly improved uterine tension in both pregnant and non-pregnant women. Xu found that injections of earthworms induced more contractions in the mouse uterus than the normal pituitrin solution (0.01 mg/ml).

## 6. Anti-cancer properties

Researchers have successfully used earthworm extracts to treat transplanted cancer in rats with S-180 cells. After an 88-day enema with an extract dosage of 5 mg/ml, the cancer dramatically shrank (Wang, 1988). As part of the 3H-TdR, used a dialysis method to separate some parts and look at how they affected MGc803 gastric tumors. The results showed that some earthworm parts could stop MGc803 gastric carcinoma from using 3H-TdR ( $p < 0.01$ ), and these parts still had the same effect after being heated to 56°C for 30 minutes ( $p < 0.05$ ). This indicates that earthworm dialysis is highly heat-resistant on a restricted scale. Sun *et al* compared four treatments—cancer cell suspension, earthworm extract, blood porphyrin derivative laser, and earthworm extracts—for their ability to eradicate cancer. The combination of earthworm extract, blood porphyrin derivative, and laser therapy resulted in the greatest incidence of depression on cancer cells. Used a chemical-luminous method to find that the earthworm extract's better ability to kill cancer by increasing blood porphyrin, a derivative laser, is because it has more active oxygen. China has created a novel anticancer medication called "FU NAI KANG," which is based on earthworms.

## 7. Earthworm extracts have the ability to kill or stimulate sperm

Earthworms' succinic and hyaluronic acids can cause agglutination, which can kill sperm documented earthworm toxicity. Earthworms had up to 200 parts per million of arsenic, according to the findings. Washing can reduce arsenic toxicity, and studies involving rabbits, rats, and dogs given enemas or intravenously injected with earthworm extracts showed a relatively low level of toxicity. The degree of toxicity and adverse effects is not detrimental to human health. China may employ earthworms' ability to destroy sperm as a method of family planning.

### Use of earthworms in medicine

#### 1. Clinicians have used earthworms to treat the following illnesses

##### 1.1. Managing Bronchial Asthma and Tracheitis

For bronchial asthma treatment, administered fried hot earthworm powder orally three to four times a day at a dosage of three to four grams each. We treated 44 asthma patients with an earthworm concoction known as "Chuan-shu-ning pill," and 84.09% of the patients showed positive response to the therapy. Long-lasting and mild asthma relief is a hallmark of this approach (Ling, 1961). In 275 instances of bronchial asthma, a single earthworm injection resulted in a complete recovery for 78% of patients; the therapeutic results were more favorable for children than for adults. Huang Wenda's study used a 30% earthworm injection to treat both adult persistent asthma and children's asthma. The adults' dose was 2 ml, and the children was 0.1-2 ml, given once a day after the onset of asthma. The breathing improved after ten to thirty minutes of therapy. Asthma's distinctive noises subsided, and phlegm production became effortless. Asthma symptoms completely vanished after two to four sessions. Typically, adults received intramuscular injections of 1 milliliter (or 1 gram) of earthworm extract preparation on the first day, then 2 milliliters every day if adverse effects did not manifest on the first day.

The Internal Medicine Department of Jiangsu Hospital deemed a ten-day course of treatment complete in 1971. Multiple tests showed that mixtures of many earthworm species were more beneficial in treating 101 cases of hot asthma than concoctions derived from a single species. In 88.1% of patients, a daily dose of 2 ml intramuscular injection of earthworm extract given every other day resulted in responses within 1 to 2 weeks. Microbiological tests and germ culture findings have demonstrated the ability of earthworm tissue components to repair mucosal membranes and reduce tracheitis-induced inflammation. Treating 100 children with asthma with earthworm powder, particularly for hot asthma, yielded excellent outcomes.

##### 1.2. Management of epilepsy

An effective treatment for epilepsy was an earthworm pill made from a family recipe that was handed down through the centuries and largely consisted of earthworms (*A. caliginosa*). Zhu (1983) developed a mixture of 3-6 g earthworms, administered once a day, to treat 20 partial epilepsy sufferers. Zhu (1983) found that of them, 16 instances had full recovery, 3 had improvement, and 1 had no change at all. Zhang used a different earthworm extract, administered once daily for 10 to 20 days, to treat 12 patients with epilepsy. Five patients had no episodes for six

months; four patients had no epileptic episodes for a year; and the attack times of the other patients showed a discernible decline (Zhang, 1984).

### 1.3. Management of hypertension

Administering an earthworm extract tincture twice daily at a dose of 20 milliliters proved to be a successful treatment for 34 patients with hypertension who had previously undergone ineffective treatment with a variety of drugs. High blood pressure often dropped 4–10 days after starting this earthworm treatment. Eleven cases of hypertension received an earthworm extract known as "Earth Dragon B1" three times a day and two milliliters once; the results showed an effective ratio of 90.9% for the decrease of hypertension without any noticeable side effects. Huo reported that a combination of earthworm extracts effectively treated 17 cases of hypertension. We achieved an 86.6% improvement rate in 30 patients with high blood pressure by intramuscular injection of an earthworm-derived K factor. Additionally, the injection demonstrated a depression function in various phases of hypertension and worked better for controlling high blood pressure than the majority of pharmaceutical therapies.

### 1.4. Managing schizophrenia

People reported using earthworms to treat 110 cases of schizophrenia. We divided these patients into two groups: In the first group, 60 patients received therapy with earthworm powder, while 50 patients received treatment with an injection of earthworm extract in the second group. 18 patients in the first group and 11 in the second group showed improvement throughout the course of a 60-day therapy program. Fresh earthworm materials proved to be more effective than dried ones.

### 1.5. Management of Ulcers in the Legs

We treated 50 instances of leg ulcers with an external application of earthworm ointment, known in Chinese as "Xin-fu-Shuang." Of these, we completely recovered 17 cases and showed improvement in 37 others. It had the following effects: it reduced pain, eliminated pus, disposed of rotting tissues, and enhanced the development of muscle buds. Applying a syrup containing powdered sugar and earthworms to the ulcers yielded positive results. We also treated leg ulcers orally with earthworms. We used this method to rinse the earthworms with cold water and soy milk. I took this just before supper. After taking 300 earthworms, the patient entirely recovered.

### 1.6. Mumps Treatment

After cleaning, we placed the earthworms in a container, added the same amount of powdered sugar, and immersed them. We applied the yellow-white mucus to the damaged areas and covered them with gauze, which the earthworms gradually released. We replaced the mucus every two to three hours. Because of its quick detumescence and anti-fever effects, observation of 20 cases demonstrated that this was a more effective way to treat mumps. This approach successfully treated 170 cases of mumps within 1 to 3 days.

### 1.7. Treatment for Eczema, Urticaria, and Anaphylaxis conditions

In 35 instances of dermatitis, thirteen patients showed complete recovery, thirteen showed improvement, five

showed response to therapy, and three showed no improvement after receiving injections of earthworm tissue extracts at acupoints. After applying a sample of 60 g earthworms and 30 g sugar, the patients made a full recovery. They applied the mixture to the affected area four to five times a day. Hu (1980) reported that this technique treated recurrent episodes of eczema and cutaneous clonic itches.

Earthworm injections, administered once a day at a dosage of two milliliters each, effectively treated eighty-four percent of the 100 cases of urticaria. After fifty more cases of therapy with this strategy, fifteen patients recovered, twenty-four improved, nine reacted to the treatment, and two had no effects at all. To stop strip bleeding, we used external glycerine extract and earthworm liniment. Three of the nine patients recovered fully in three days, while one patient required four to ten days to recover. We pulped fresh earthworms using chives' roots. We uniformly combined the earthworm pulp with sesame oil. We recovered 26 cases of strip bleeding using this procedure, according to reports. Earthworms can also treat regular lupus erythematosus. One step in the procedure included mixing powdered sugar and fresh earthworms to create an infusion. After two to four sessions, we successfully treated fifteen patients by administering the infusion to the afflicted regions.

### 1.8. Care for Burns and Scalds

To make an infusion, we soaked a sample of fifteen earthworms in a sugar solution for 10 hours. Applying this earthworm infusion topically to the injured skin resulted in the cure of fifty cases of burns and scalds, ranging from 10 to 110, within a week. Another account describes agitating an earthworm-sugar solution by combining 60 g of sugar, 120 g of dried earthworms, and a small amount of borneol. Most of the time, applying the solution four to six times to the burned or scalded leg over a day resulted in the wound healing in five to seven days without any obvious scars or unfavorable side effects. The traditional Chinese medicine, Burn Ointment 101, combines tissues from *Allolobophora caliginosa* with other medicinal plants. 98.7% of the 5011 instances of first- and second-degree burns and scalds that received this treatment fully recovered. Twenty-three out of the thirty-two cases of severe burns and scalds fully recovered.

### 1.9. Handling of Breaks

Using earthworm extracts, we treated sixty-three cases of femur fractures; the tumescence disappeared in twenty-four hours, the discomfort subsided in an hour, and the bone healed satisfactorily over an average of 38.7 days. Li examined 264 new cases of femur stem fractures (within 7 days) and found that, in comparison to other therapies, the healing time of fractures was 3.6 days shorter after earthworm treatments ( $p < 0.05$ ). Li suggested that this activity might be associated with the lipid and nucleic acid content of the earthworm bodies.

### 1.10. Therapy for Erysipelas

By applying a mixture of fresh earthworm tissues and red sugar to the affected areas, eleven patients with erysipelas recovered in three to five days.

### 1.11. Management of Encephalitis B Sequelae

An extract from stewed fresh earthworms treated ten cases of encephalitis B sequelae, and the patients responded well to the therapy.

### 1.12. Treatment for Apoplexy Due to Blood Deficiency

The reported that administering fresh earthworm extracts to treat 381 instances of blood-deficiency apoplexy resulted in an average effective cure rate of 79%.

### 1.13. Therapy for dizziness

We used an extract from a combination of earthworm tissues to treat vertigo. Twenty out of the 32 treatments resulted in complete recovery, seven demonstrated improvements, two reacted to the therapy, and three showed no change at all.

### 1.14. Management of Hematuria and Hematemesis

A yellow fluid emerged from the earthworms' body pores when we combined 50 new earthworms with 250 g of red sugar. Within two hours of taking this secretion orally (20 milliliters per therapy), the patients' blood spitting ceased. After consuming 100 milliliters of secretion, the illness fully recovered.

### 1.15. Handling of Intestinal Ulcers

An oral dosage of dried earthworm powder (two grams, three to four times a day) completely healed 34 cases of digestive ulcers and improved 6 cases.

### 1.16. Handling Vesical Calculus

Chen (1987) reported that using earthworms to treat five cases of vesical calculus of cystolith resulted in notable therapeutic benefits.

### 1.17. The Internet's Immune System

Animals' immune systems have developed to defend them against infections, microorganisms, viruses, and diseased cells. Generally speaking, lymphocytes and phagocytes are the two types of cells that mediate immunity. Even though earthworms don't seem to have lymphoid organs, lymphocytes, or immunoglobulin, their body fluids do contain many humoral defense factors, including bactericidins, lysosomal enzymes like acid phosphatase, and agglutinins (e.g., lectin), which all work together to make their immune system powerful (Cooper, 2005) [6]. Earthworms mediate through innate immune responses and possess basic, non-specific recognition mechanisms. Because of their powerful physicochemical barriers, earthworms serve as the first line of defense against infections. During an infection, dorsal pores expel a collection of leucocytes, known as coelom, which are free inside blood vessels or fluid-filled bodily cavities. These leucocytes adhere to the bacteria, engulf them, and ultimately destroy them. The earthworm's leucocytes, often referred to as coelomocytes, are in charge of innate immunological processes such as phagocytosis and encapsulation to protect the body against infections and parasites. Due to their slower habits, the worms are able to assess potential threats. In addition to its immunological function, coelomic fluid maintains the body's surface moisture, which makes the burrow wall slick, smooth, and simple for the worm to move about in. Polymorphonuclear

neutrophils, macrophages, and monocytes categorize leucocytes, also known as phagocytic cells.

According to Stephenson's 1930 writing, the coelomic corpuscles consist of (i) amoebocytes, which are spheroidal and have a diameter of 15-20 $\mu$ . They have a large oval nucleus and a group of very large pseudopodia, which resemble stretched-out petals. The nuclei are oval-shaped and big. (ii) Vacuolar lymphocytes, which are discoidal, irregular, and non-amoeboid cells that may enlarge to 50 $\mu$  in diameter. (iii) Spherical or ovoid eleocytes, which may have an average diameter of up to 50 $\mu$  and sometimes as much as 80 $\mu$ . Only a coating of fatty globules can unstretch them, revealing their translucent nature. These eleocytes lack a nucleus; instead, filaments shoot outward from the centrosphere to the cell's periphery. There are lens-shaped, non-amoeboid mucocytes that can be up to 100 $\mu$  wide and don't have any inclusions. There is also a large hyaline area with a big nucleus in the middle, as well as groups of very reflective globules. Kurek and Plytycz (2003) divided coelomocytes into three groups: (a) eleocytes, which have big chlorogosomes; (b) granular amoebocytes, which have granular cytoplasm; and (c) hyaline amoebocytes, which do not have granular cytoplasm. In addition to their involvement in clotting and wound healing, coelomocytes are crucial in the identification and removal of foreign materials (Cooper, 2002) [9].

## Biological Activity

### 1. Antioxidant activity

An antioxidant is a molecule that interacts with free radicals and other active oxygen species within the body to prevent oxidation processes from harming other compounds. Since one antioxidant molecule can only react with a single free radical, the supply of antioxidants remains limited. Consequently, the need to replenish antioxidant resources whether naturally occurring or via supplements never goes away.

### 2. Reaction of Earthworm to Oxidative Stress

Earthworm tissues contain large amounts of antioxidants such as reduced glutathione (GSH), glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD). This explains why earthworm paste and its extracts can fight oxidative damage. We examined the antioxidant activity of the tissue homogenous-glycolipoprotein (G-90) extract of *Eisenia foetida* in lab-grown human fibroblasts and epithelial cells. Researchers discovered that this extract exhibits an antioxidant action by repairing tissue (Grdisa *et al.*, 2001). Balamurugan (2006) demonstrated that earthworm paste from *Lampito mauritii* can decrease lipid peroxidation in albino rats and boost liver antioxidants like GSH, GPx, CAT, and SOD.

### 3. Earthworm Anti-Ulcer Properties

Stomach-related discomfort is a frequent clinical symptom linked with both organic and functional dyspepsia. Peptic ulcer disease, a prevalent gastrointestinal ailment in clinical practice, might be the cause of organic dyspepsia. An increase in acid and pepsin production, as well as a loss of mucosal resistance, appear to be the primary causes of peptic ulceration. *Helicobacter pylori* is a gram-negative bacillus that thrives in the stomach and duodenum and lowers mucosal resistance. Over the last 25 years, there has been a significant breakthrough in the pathogenesis and management of duodenal and stomach ulcers. One effective treatment for peptic ulcers is to protect the gastro-duodenal mucosa, inhibit acid secretion, and neutralize stomach acid.

#### 4. Effect of Earthworm Paste/Extract: Anti-Inflammatory

**Inflammation:** Inflammation is a defensive reaction that occurs locally and is brought on by tissue damage or injury. It works to wall off the damaged tissue as well as the causing factor. Inflammation is characterized by redness, swelling, heat, and discomfort. Inflammation has some positive aspects, such as killing invasive bacteria and sealing an abscess chamber to prevent inflammation from spreading. A lot of things happen at once, like fluid leaking out, white blood cells moving into the area of inflammation, and arterioles, capillaries, and venules getting bigger, which makes them more permeable and increases blood flow.

A few writers have established the anti-inflammatory properties of earthworm paste and its extract, including Balamurugan (2006). In 1987, Yegnanarayanan and colleagues discovered that the petroleum extract and ethanol of the earthworm *Lampito mauritii* have anti-inflammatory properties in albino rats. We gave the animals cotton pellets to induce paw edema and granuloma. When carrageen was used to make albino rats swell up, petroleum ether percentage of total earthworm protein from *L. mauritii* and found that it helped reduce inflammation. Balamurugan (2006) demonstrated that earthworm paste inhibited carrageen exudates and swelled rats' paws. He also demonstrated that the granulomatous growth occurred during the chronic phase of the granuloma.

#### 5. Interaction of Earthworm Extract on Cancer

Uncontrollably dividing cells that have the potential to spread to other bodily areas are known as cancer. One of the many different types of cancer can affect almost any portion of the body. Lombricine, a skin extract from *Lumbricus terrestris*, can stop SHN mice from getting mammary tumors. Hrzenjak *et al.* took "glycolipoprotein-G-90" from homogenized whole earthworm tissue (*Eisenia foetida*, *Lumbricus rubellus*) and discovered that it stopped mouse cells from turning into tumors while they were still alive. Before, Hrzenjak *et al.* (1998) looked into how the P I and PII parts of G-90 affected human cell lines in the body. They used MiaPaca 2 (pancreatic carcinoma), HeLa 9 (cervical carcinoma), and W138 (normal fibroblast).

#### 6. Earthworm's coelomic fluid exhibits antibacterial activity

An antibiotic is a chemical that, at low concentrations, either kills or suppresses microorganisms. The coelomic fluid and tissue extract of earthworms show potent antibacterial properties. Many earthworm extracts are effective against a variety of pathogenic and non-pathogenic bacteria, including *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, and *Escherichia coli*.

#### 7. The earthworm extract (G-90) has anti-coagulative activity

An anticoagulant is a chemical that inhibits blood coagulation. Different blood samples have shown the anti-coagulative and fibrinolytic effects of earthworm extract G-90. In G-90, which they extracted from the tissue homogenate of the earthworm *Eisenia foetida*, two serine proteases, PI and PII. They said that these enzymes could break down fibrin clots in the blood of people with cancerous tumors. Researchers Popovic *et al.* (2001) found two proteolytic enzymes (PI and PII) in *Eisenia foetida*'s G-

90. They then saw that these enzymes broke down blood clots from dogs with heart problems and cancerous tumors. Pesticides are detrimental to the natural world and are thus regarded as toxic to the environment (Murugesan *et al.*, 2021) [23]. Chemical pesticides, comprising herbicides, fungicides, rodenticides, and insecticides, pose a serious threat to biodiversity and the environment, contributing to air and water pollution (Murugesan *et al.*, 2023) [22]. Many are turning to natural alternatives over synthetic counterparts in pursuit of safety and stability (Murugesan *et al.*, 2021) [24]. Traditional medicine is also a vital source of potentially valuable compounds for the development of therapeutic agents (Kaleeswaran *et al.*, 2019) [15]. Plant extracts and secondary metabolites have emerged as promising alternatives to synthetic pesticides (Rengarajan *et al.*, 2024) [34, 35], offering potential solutions for sustainable pest management strategies (Murugesan *et al.*, 2024) [21].

#### Conclusion

A variety of medical purposes may utilize the enormous pharmacological potential of earthworms. Traditional Southeast Asian medicine has long recognized the therapeutic effects of its proteins, peptides, enzymes, and immunoprotective substances. Studies have demonstrated the lytic, immune-stimulating, and clot-dissolving characteristics of earthworm extracts. Recent research has focused on fibrinolytic enzymes from species such as *Lumbricus rubellus* and *Eisenia fetida*. These enzymes may be able to help treat illnesses related to thrombosis. Earthworm extracts also exhibit a number of additional bioactivities, such as wound-healing, antibacterial, anti-inflammatory, and anticancer effects. These findings imply that earthworms could be a useful source of organic compounds for the development of novel medications and treatments, necessitating further investigation into their pharmacological characteristics.

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#### Compliance with ethical standards

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#### Data availability

Open for all

#### Availability of data and material

All the collected articles and their data are enclosed in this article in the reference section.

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