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Complementary Review Of Anti Arthritis Activity Of Pithcellobium Dulce Plant Extract

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disorder. It generates joint inflammation and synovitis. Which influence more or less 20 % of the population in India. The arthritis symptoms are created step by step. The major symptom of RA is a pain in the joint. The high level of rheumatoid factor (RF) in the blood is most often associated with autoimmune disease such as rheumatoid arthritis & sjogren's syndrome. The Normal range of RF is from 0-20 IU / ml. The anti-arthritis activity evaluation can be studied by using an animal model. The anti-arthritis activity can be done using pithecellobium dulce leaves. The pithecellobium dulce is also called Manila tamarind. PD leaves are also used as astringent to treat antidiabetic activity. The phytoconstituent is existing in leaves are alkaloids, phenol, afezilin, glycoside, saponin, telephenoid, quericitin, dulcitol and laempferol. The fresh leaves are collected and dried to prepared the extract. The dried leaves were ground by using a blender has fine powder. In pithecellobium dulce leaf extract, various methods of extraction like methanol, ethanol, and aqueous extract used for many activities such as CNS depressant, Analgesic, Antidiarrhoeal, Anti-inflammatory and Anti arthritis activity. The ethanol extract of pithecellobium dulce has a significant Anti arthritis activity.



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INTRODUCTION

Rheumatoid arthritis (inflammation of joints) is a chronic, progressive, inflammatory, autoimmune disease, mostly act on periarticular tissues and joints. The pathological process is Tigger by antigen-antibody complexes. Mediators attributed

to inflammation released, rising joints begins the inflammatory process. In initial lesion formation exists vasculitis, through secretion hydrops along with inflammatory cells combined with infiltration. The unharness of lysosomal enzymes on inflammatory cells that bring harm towards bones as well as animal tissue ends up in disabilities. These are caused by an additional range of proinflammatory molecules free from macropages, including reactive chemical element species and ecosanoids. Ecosanoids such as prostaglandins, leukotrienes are secreted by immune cells and macrophages (Shin *et al.*, 2003). Enzymes such as Lox and Cox for a chronic inflammatory defect on a potential target, so the arachidonic acid metabolism of modulation is completed via inhibiting the enzymes of Cox and Lox (Kore *et al.*, 2011).

RA is a group of process, including the formation of pannus and cartilage, proliferation of the synovial cell, bone destruction and fibrosis. This process

exist mediated via group enzymes such as cytokines, prostaglandins and proteolytic enzymes. Any age of people can be affected by RA. The usual onset of age is between 25 and 50, with a high in the 40s and 50s (Shivanand, 2010). In India, about 20% of the population were suffering from arthritis. The most common affected joints by arthritis are weight-bearing joints includes knee joint, feet joint, hip joint, spine joint, finger joint and thumb joints. The four main groups of drugs used in the treatment of arthritis are analgesics, disease-modifying anti rheumatoid drugs (DMARDs), NSAIDs and corticosteroids (Patwardhan et al., 2010). Despite treating arthritis by NSAIDs and other drugs, the search for newer drugs has been continuing because the available synthetic drugs have a lot of limitations. The Ayurveda and herbal medicines have also started admitting by modern medicines. Herbal medicine has a more positive influence on the treatment of RA. This paper deals with the study of the anti-arthritis activity of pithecellobium dulce leaf extract.

Rheumatoid Arthritis Can Be Classified As Follows

1. Septic arthritis
2. Palindromic arthritis
3. Juvenile arthritis
4. Rheumatoid spondylitis
5. Other sorts of rheumatoid arthritis

Osteoarthritis – (Gabriel et al., 2003) It can be further classified as, Primary and secondary osteoarthritis. Where Primary osteoarthritis occurring in older peoples. And secondary osteoarthritis affects at any stages.

Further classified based on causative agents

1. Arthritis caused by a bacterial infection in joints are suppurative arthritis
2. Arthritis caused by bacteria Mycobacterium tuberculosis are Tuberculosis arthritis
3. Arthritis caused by Lyme disease is Lyme arthritis
4. Arthritis caused by Pathogenic Viral infections are Viral arthritis

Epidemiology

The overall worldwide generalite RA anciently evaluated while 0.24 % dependent on the Global Burden of Disease 2010 Study (Cross et al., 2014).

Evaluations of RA predominance on northern European nations and the United States exists ordinarily higher; usually intermediate of 0.5 to 1% (Myasoedova et al., 2010; Hunter et al., 2017). The annual rate of RA within northern European nations and the US occur evaluated roughly forty for every 100,000 people (Myasoedova et al., 2010; Eriksson et al., 2013).

Most epidemiologic investigations of RA have been directed in the United States or northern European population. Subsequently, epidemiologic estimates of RA and distinguishing proof of hazard factors come generally from these population. The frequency and commonness of RA are a lot more prominent in a certain population, for example, in the Pima Native Americans, where rates are up to multiple times higher than those of most population bunches (Puente et al., 1989).

The RA comprises liking towards influence ladies, whose occurrence predominance RA rates arise twice while high in men. The lifespan hazard is creating 3.6 per cent of RA in ladies as well as 1.7 per cent in men (Crowson et al., 2011).

Etiology

In the RA analysis as yet neither familiar, the helplessness of genetic during mix towards impact attributed to backdrop factors most likely requirements since, RA beginning. The components are as follows:

Factors on Environment

There are predictable data showing that smoking could boost the advance of positive RF, Damaging RA people who positive on HLADRBI/SE. RA is attributed to starting musty connected along with oxide presentation, paraffin oils, blood bonding, and dietary factory.

Effect of steroids

A more number of women than men are influenced by RA, especially at younger ages. This implicates a plausible role for sex hormones in powerlessness and pathogenesis. In women, the top rate is seen in the perimenopausal, postpartum period and pregnancy.

Hereditary components

Rheumatoid joint pain has a genetic connection, and the ailment can run in families. Individuals with explicit human leukocyte antigen (HLA) genes have a more noteworthy possibility of creating rheumatoid joint inflammation than individuals who don't have the HLA genes. All things considered, not every person with the HLA genes create rheumatoid joint arthritis.

Symptoms

Indications of arthritis are step by step created. The first side effects over small joints frequently, for example, fingers, legs and elbow, despite certainly such on shoulders with knees, might be determined yet and muscle firmness can be a prominent yet features.

Symptoms of RA incorporates.

1. Morning solidness that keeps going for at least 1hr.
2. Joint pain, besides inflammation, heat, delicacy, along with solidness, attributed to joint once relaxing.
3. Low-grade fever.
4. Inflammation of small veins can cause small nodules under the skin, but they are painless.
5. Loss of weight.
6. Sleeplessness.
7. Fatigue.
8. Weakness of muscle.
9. Inability to utilize hand or walk

Pathophysiology

Rheumatoid Factor

In RA, a well-known autoantibody is RF (Rheumatoid Factor). RF has restricted particularly, it can also consider in healthy controls and patients combined with other autoimmune diseases Like systemic sclerosis and systemic lupus erythematosus and disease of non-autoimmune diseases, like will- cer and chronic inflammation.

RF exist as outlined while immunoglobulins category (IgM, IgG, IgA) regulated anti-Fc region of IgG.

Totally non-identical isotypes of RF will arise to diagnosed based on immune globulin exits as such max current (Ingegnoli *et al.*, 2013). IgM is high titers and the IgA are concept intended extremely expressive of RA (Dorner *et al.*, 2004).

Nonetheless, The RF levels decrease frequently were observed in patients effectively treated along with disease-modifying anti-rheumatic medication (DMARDs) (Figure 1) (Ingegnoli *et al.*, 2013).

The immune composite concept toward push stimulating assembly proceeding from unhealthy cytokines of inflammation. Comparable to growth death factor (TNF) α (Mathsson *et al.*, 2006).

Anti- Citrullinated Protein Antibodies (ACPAs)

The autoantibodies are regulated against proteins or peptides of citrulline residues. Citrullination exists as invariable post-conversion alteration of arginine such is mediated through enzyme termed as (PADs) peptidyl arginine deiminases leads to cell death. The activation of PAD as a result of a concentration of high intracellular calcium throughout necrobiosis is able to push for the citrullination of target Associate in Nursingtogens. Any dysregulation of programmed cell death or an incapable clearance based on apoptotic cell remnants could also exist concerned within the malfunction of self-toleration because of aggregation of dying cells with ensuant approachable of intracellular antigens. It may assist citrullinated proteins of meeting with the system resulting in antibody creation in generative susceptible separates (Katekhaye and Nagmoti, 2013). This can ultimately lead to the immune complicated organization, upregulation of unhealthy cytokines is followed, that is thought to be the thrust of the chronic inflammation such typical of RA (Valesini *et al.*, 2015). In ACPA present ascertained being for a long time symptomless people with don't essentially result in RA development (Majka *et al.*, 2008). At a length of the opposite side, within independently affected by contractor manifestation together with the pain of joint. (arthralgia), the RA is the enlargement of prophetic in the presence of ACPA (Bos *et al.*, 2010).

Evaluation Of Anti Arthritis Activity Using Animal Model

Paw Edema Induced By Carrageenan

Carrageenan induced paw edema in rats (CRR) is extreme usually utilized in an animal model. CRR give rise to terrible and chronic inflammatory reactions. The terrible reaction seems to be like rheumatoid joint inflammation injury plans, which are portrayed by sustained cellular emigration (Kim *et al.*, 1999). Hydrolysed Carrageenan induces joint inflammation by inhibiting DNA synthesis. Additionally, impacts on acetate de chrome delivery and cell biology set back cell formation that created and cell passed away (Shivanand, 2010).

Procedure

1. Weigh the animals & number them.
2. Make a mark on both left and right hind paws so that every time the paw is dipped in Mercury, column up to the fixed mark to ensure constant paw volume.
3. Note the initial paw volume of each rat by the method of Mercy displacement.

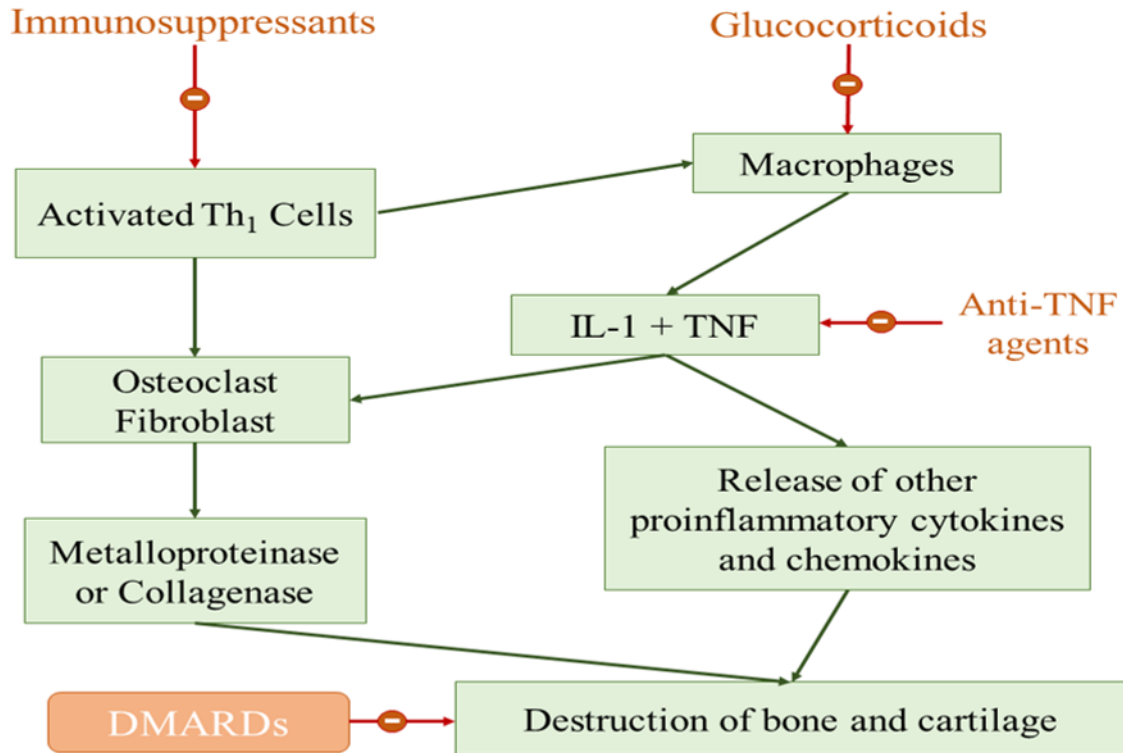


Figure 1: Pathophysiology of Arthritis

4. Divide into 2 groups of animal, each group comprising at Least 4 rats. one group inject saline and other groups inject indomethacin subcutaneously.
5. The 0.1 ml of 1% w/v carrageenan injected after 30 mins in the plantar region of the left paw of control as well as indomethacin - treated group. The right paw will serve as a reference for non - inflamed paw for comparison.
6. Note the paw volume of both legs at 15, 30, 60 & 120 mins after the carrageenan challenge.
7. Calculate the % difference in the right & left paw volumes of each animal.
8. Compare the mean % in paw volume & express as % oedema inhibition by the drug.

Monosodium Urate Crystal-Induced Arthritis

Principle

Uric acid is the unmetabolised product of purine which is deposited in the diarthrosis joint which elicits initiation of kinin leukotriene B₄, neutrophil granulocytes cumulation described by intermediate criticize of terrible Arthritis or Gouty arthritis. This rule exists infused interdermal along genu turn out joint inflammation.

The salt on gouty arthritis is salient. Therefore the accumulation of metallic element ill tophi is notable on urate. Suspensions of sodium urate crystal of 20 mg are injected in knee joint of their own. It encountered serious ache Associate in Nursinged exhaustion that took when an acute gouty attack (Faires and Mccarty, 1962).

Procedure

The suspension of endotoxin-free monosodium urate crystal of (4 mg) 0.2 ml by intradermal infusion through right food pad, inflammation is induced. Day 0-3 as considered. MSU is treated before half an hour of both test & standard from the begun of day zero and proceeded towards further 3 days (Rasool and Varalakshmi, 2006).

Preparation Of Monosodium Urate Crystal-Induced Arthritis

The uric acid has been dissolved around 4 g and boiled with (9 ml/0.5N) of NaOH with water of 800ml, modified pH 8.9 at 60°C; placed in a cool room for overnight to cooled; then wash and dry. The sharp point of crystals has been formed and made suspended on clean saline of 20mg/ml. Before handling the MSU, crystals were examined for bacterial endotoxin adulterate utilizing a pack of Limulus ameobocyte lysate (LAL) as a trade test shown by a distributor (Sabina et al., 2010).

Formaldehyde Induced Arthritis

Principle

The oedema is considered as a Swelling around the lower leg joint and the arthritic rat paw is of Particular tissue (Kim *et al.*, 1999). As a result of histamine release, serotonin and the site of infusion of prostaglandin, oedema is developed, followed by the injection of formaldehyde to the rat (Buadonpri *et al.*, 2009). Formaldehyde induces joint inflammation on the handling site by protein reconstruct. It generates an immunological response in the case of downgrade results (Kore *et al.*, 2011).

Procedure

1. Divided into four groups of animal each group contain 6 animals, where Group A is supplied 0.5% of CMC meet with controlled. Group B undergo Indomethacin 10 mg/kg give out standard, Group C and D served test solution.
2. 0.1 ml of formaldehyde to an animal in sub grower outside left hind paw, on first, as well as the third day, attributed to test.
3. For 10 days, both the test towards standard are handling at one time per day as orally.
4. In present, interference aim to increase in paw oedema for each category is evaluated at a length of 10days along differentiated in addition to standard. Paw oedema is estimated by using digital vernier callipers or plethysmometer (Telang, 1999).

Arthritis Induced By Pristane

In this method, rat serves as chronic by PIA, symmetrical model such mimic a large number of the aspects of the human infection. PIA, along with the mineral oil pristane, is induced in susceptible rats. Disease side effects begin to show up after 7-10 days.

The examination can be ended around day 30 after induction. PIA is T cell-driven and depends on MHC in any case. So far, no antigen has been identified in PIA.

This disease is additionally transferrable by T cells permitting direct investigations of T cell arthritogenicity *ex vivo* (Wilder *et al.*, 1999).

Oil-Induced Arthritis (OIA)

OIA grows around 14 days after the intradermal infusion of IFA. In this, a middle monophonic joint inflammation creates in the hind paw and lower leg, which can progress to the front paws. Disease dies down before day45 (Kleinau *et al.*, 1991).

Arthritis Induced By Streptococcal Cell Wall

An intraperitoneal infusion attributed to cell wall peptidoglycan-polysaccharide by aqueous suspension fragment since streptococci and a few different sorts of bacteria into susceptible rat strain, male Lewis rodents, induces extreme erosive joint inflammation. An acute, thymic dependent, Compliment-subordinate stage creates within 24h (Wilder, 1988).

Aureus-Induced Septic Arthritis

To induce joint inflammation, the intravenous infusion of live microscopic organisms (*S.aureus*) suspension is given to a susceptible strain of mice in the parallel tail vein of each mouse. To assess the intensity of joint inflammation, a clinical scoring (arthritic index) is utilized as previously described (Paola and Cuzzocrea, 2008).

Collagen Type Ii Induced Arthritis In Rats

Principle

Type II collagen was induced arthritis in rats. The RA models are utilized by the CIA. It is hereditarily composed of Class II major histocompatibility complex (MHC) molecules. The great method to examining a mechanism of basic immune reactions to human disease which engaged by autoantigen potential. Collagen joint pain can be induced in numerous strains by vaccinating to rat with an emulsion of complete Freund's adjuvant and type II collagen.

The illness, which defined through the elaborating of both humoral immune response along with cell to collagen type II, as it may be latently the lymph node cells and sensitized spleen were transferred, IgG antibodies until type II collagen. Certain discoveries arise predictably besides the suggestion the type II collagen of arthritis is a result of immunologic hypersensitivity. A current result indicated which adjuvant rat joint inflammation expose both cell sensitivities and humoral towards collagen type II homologous. While brought among the dermis, The antigen-presenting cells (APCs) is captured quickly by CII. Unwellness includes the antigen-specific and auto ractive which shows by the activation of B and T cells. The T cell-derived cytokines and T- lymphocyte promotes separation and trigger macrophages, osteoclasts and fibroblast, prompting the forceful erosive arthritis (Doncarli *et al.*, 1997).

Procedure

1. Dissolved the 2.0 mg/ml of collagen of 0.1M concentration of acidic acid. Kept it at 4°C overnight.

2. To an equivalent, the mixture is added drop by drop. volume of chilled incomplete Freund's adjuvant.
3. Each rat gets 0.5 mg collagen in 0.5 ml on day zero. Similarly, 5 sites are divided. The infusions on intradermal, every appendage as a base of one. Other is nape to the neck. postimmunization for 7 days, the animals get similar booster infusions. Animal receive just control of incomplete Freund's adjuvant, which is acidic acid of diluted with 0.1 M.
4. The size of both paws serves estimated plethysmographically at day 20. The limit of chance the incorporating animal towards minimal transient disease, which animal having paw volume as 1.8 ml or more prominent is utilized for the upcoming test.
5. The animal receives the test p.o. from day 20-40. one time per day at a length of 41 days, the paw volumes are recorded once more (Doncarli *et al.*, 1997).
4. Intentionally since the day of the thirteenth to twenty-first st, the animals have not been dosed of a test or the standard compound (Butler *et al.*, 1992).

Arthritis Induced By (Comp) Cartilage Oligomeric Matrix Protein

1. IFA induced by Immunizations with COMP of extreme joint inflammation in defenceless strains of rat, ie. LEW and DA (Ling *et al.*, 1988; Carlsen *et al.*, 1998).
2. Despite the fact that the joint inflammation on peripheral in clinically looks like RA, joint inflammation is induced by COMP, in any case, doesn't ensure in a constant account of joints.
3. It seems disease increasing, by all accounts, to be subject to a resistant reaction until COMP autologous along with not on hybrid sensitivity, until other ligament collagens rat (Newbould, 1963; Rosa, 1972).

Complete Freund's Adjuvant Induced(Cfa) Rheumatoid In Rats

Principle

In the rat method, the joint inflammation was induced by Complete Freund's adjuvant. Which is generally utilized test method for joint inflammation towards clinical and the laboratory features that mimic the highlights of human arthritis disease in clinical. The anti-inflammatory and immune inhibiting drugs are highly sensitive in this method and applicable towards investigation to pharmacological control on inflammation process and pathophysiological along with estimation to antinociceptive capability for drugs (Newbould, 1963; Pearson and Wood, 1963).

Procedure

1. Animals are infused towards sub plantar region on day zero of the left rear paw with (CFA) complete Freund's adjuvant of 0.1 ml.
2. It comprises suspended Mycobacterium butyricum on substantial paraffin oil according to grinding motor and pestle of 6mg/ml concentration.
3. The test towards standard are dosing is administered around the equal time is proceeded to the length of 12 days as indicated by accompanying record.

Pithecellobium Dulce

Pithecellobium Dulce belongs to the family fabaceae (leguminasae). It is also known as manila tamarind. It is a medium-sized evergreen, having a height of up to 118m. It is grown all over India and in Andaman and tropical America. It is also called vilayati babul (Hindi), kodukkapuli (Tamil), illach-hunchi Kai (Kannada), ambli (Gujarat), jilabi (Bengali) and foreign tamarind (Marathi). Pithecellobium Dulce has many uses. The bark of this is used as an astringent in the treatment of dysentery, febrifuge and also in dermatitis and in inflammation of the eye. The leaves of this are used as an astringent, emollient, abortifacient and antidiabetic activity. The roots of this have estrogen activity. The phytoconstituent present in seeds like glycoside, glycolipids, polysaccharides, phospholipids, saponin and lipids. The phytoconstituent existing in the bark are tannins. The phytoconstituent present in leaves is phenol, alkaloid, glycoside, saponin, terphenoid, quericitin, laempferol, dulcitol, and afezilin. The plant is used for hundreds of years in Ayurvedic medicine with no reported toxicity (Katekhaye and Nagmoti, 2013).

MATERIALS AND METHODS

Plant material

Pithecellobium Dulce leaves were collected from the district of Tamilnadu, kancheepuram, in India. The leaves were carefully taken and damaged, affected

and microorganisms leaves were removed. An extract can be prepared by using dried and fresh leaves. The leaves were taken and dried out at room temperature for ten days and grinded into a fine powder using a blender.

Preparation Of Extract

Methanol Extract

The shade dried and grinded leaves or flowers or roots of *Pithecellobium Dulce* (2g) were taken 100ml of methanol in a 250 ml round bottom flask was added and extracted by continuous extraction technique using a Soxhlet extraction apparatus. After removal of solvent from an extract in vacuums, a greenish-brown colour extract was obtained.

Ethanol Extract

The shade dried and grinded leaves or flowers or roots of *Pithecellobium Dulce* were taken in a 250ml brown bottle and extracted using microwave domestic oven (microwave-assisted extraction) at 720 W with intermediate cooling using ethanol as a solvent and then the residue is separated.

Aqueous Extract

The shade dried and grinded leaves or flowers or roots of *Pithecellobium Dulce* was extracted with aqueous solvent using a continuous extraction technique. The aqueous solvent was filtered and concentrated to obtain a greenish-black residue.

Uses

1. Used as CNS depressant - a minimum dose of 100mg/kg of aqueous extract and alcoholic extract used as CNS depressant
2. Analgesic activity - The methanol extract of *Pithecellobium dulce* have significant analgesic activity.
3. Anti-diarrhoeal activity - The aqueous extract showed maximum anti-diarrhoeal activity than ethanol extract.
4. Anti-inflammatory - The methanol extract of *Pithecellobium dulce* has anti-inflammatory activity.
5. Anti-arthritis activity - The ethanol extract of *Pithecellobium dulce* has significant anti-arthritis activity.

Toxicity Studies

To determine the safe dose, toxicity studies determined on the swiss albino rat of any sex (about 20-25gm of animal weight), Age-90 days) by administering various concentration of extract which suspended in 2% of gum acacia, results show no toxicity observed till 2000mg/kg (Sugumaran et al., 2008).

CONCLUSIONS

This review shows that the pathophysiology & methods of induction of arthritis in animal studies. The plant *Pithecellobium Dulce* has a number of phytochemical constituents used for various pharmacological actions. Further investigations and research are uses to done on the plant, which may be used for the treatment of rheumatoid arthritis. This may reduce the risk of arthritis by prevents protein degeneration. The toxic dosage of plant extract is identified in the toxicity studies. It shows up to a maximum dose of 2g/kg is a non-toxic dose.

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Conflict Of Interest

The authors declare that they have no conflict of interest for this study.

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