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A Review on Safety Efficacy of Carica Papaya

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ABSTRACT:-

Dengue fever is a major public health concern in the Philippines, with hemorrhagic fever being a severe complication. The condition results in approximately 170,503 symptomatic infections and 750 deaths over a four-year period, with an incidence of about 180 dengue cases per 100,000 people and a case fatality rate of 0.44%. The primary cause of death is bleeding due to thrombocytopenia, with mortality occurring mainly among individuals under 20 years of age. Access to healthcare institutions is often limited, and hospitalization and transfusion costs are prohibitively expensive for many patients in rural areas. As a result, herbal medicines such as "tawa-tawa" and papaya are frequently used as an alternative treatment due to their low cost and easy availability. Animal studies suggest that papaya leaf extract may have therapeutic benefits. This review aims to evaluate the efficacy of C. papaya leaf extract as an adjunct treatment for dengue hemorrhagic fever through a meta-analysis of six randomized clinical trials involving 988 subjects. These trials were identified through a systematic search of PubMed, Google Scholar, Scopus, and Science Direct, and were selected based on pre-defined eligibility and validity criteria. The mean difference in platelet counts between days 1 and 5 was calculated and pooled together for analysis.

Keyword:-Dengue hemorrhagic fever, platelets, thrombocytopenia.

I. INTRODUCTION:-

Carica papaya, commonly known as papaya, is a tropical fruit tree that belongs to the Caricaceae family. It is native to Central America and Southern Mexico but is now widely cultivated in many tropical and subtropical regions of the world, including Asia, Africa, and South America.

The papaya tree can reach up to 10 meters in height and has a single stem with a crown of large, deeply lobed leaves at the top. The fruit is typically oblong or pear-shaped, with a thin, smooth skin that can be yellow, orange, or green when ripe. The flesh inside is bright orange or yellow and is filled with numerous small, black seeds.

Papayas are rich in vitamins A and C, as well as dietary fiber and potassium. They are a popular fruit for eating fresh, but can also be used in a variety of culinary applications, such as in salads, smoothies, and desserts. Additionally, papaya leaves and seeds have been used for medicinal purposes, as they contain enzymes and other compounds that have been shown to have anti-inflammatory, antioxidant, and immune-boosting properties[1-3].

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Fig.1: carica papaya

Dengue fever is a viral illness that is spread by the Aedes mosquito. The illness can be severe, and in some cases, it can even be fatal. There is no specific treatment for dengue, and the best course of action is to manage the symptoms.

Papaya has been traditionally used as a natural remedy for dengue fever in some parts of the world, particularly in Asia and Latin America. Papaya contains enzymes, including papain and chymopapain, which have been found to have anti-inflammatory and immune-modulating properties.

The leaves of the papaya plant are often used in traditional medicine to treat dengue fever. The leaves are crushed and the juice is extracted, which is then mixed with other ingredients and consumed as a tea or juice.Safety of papaya.

Carica papaya, also known as papaya, is a tropical fruit that has been traditionally used for medicinal purposes. There is some scientific evidence to suggest that papaya may have health benefits, but its safety and efficacy as a medicinal treatment have not been extensively studied.

Some studies have suggested that papaya may have anti-inflammatory and antioxidant properties, which could potentially help to reduce inflammation and oxidative stress in the body. Additionally, some research has suggested that papaya may have anti-cancer properties, and may be able to help protect against certain types of cancer.

However, more research is needed to fully understand the potential health benefits of papaya, as well as its safety and efficacy as a medicinal treatment. It is important to note that while papaya is generally considered safe when consumed as a food, there may be some risks associated with using it as a medicinal treatment, especially in high doses or in combination with other medications[4-7].

Biotonical classification:-

Carica papaya, commonly known as papaya, belongs to the following biotanical classification:

Caricapapayais a tropical fruit-bearing plant that is native to the Americas, but now widely cultivated in many tropical and subtropical regions worldwide. Here is some biotanical information about Carica papaya:

Table:- Taxonomical classification of carica papaya

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Brassicales
Family	Caricaceae
Genus	Carica
Species	Carica papaya

Carica papaya is a small, fast-growing tree that can reach a height of up to 10 meters. The plant has a single stem and a crown of large, deeply lobed leaves. The fruit is a large, fleshy berry that can grow up to 50 cm in length and weigh up to 9 kg. The fruit is yellow-orange in color and has a

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sweet, juicy flesh that is rich in vitamins A and C, as well as other nutrients.

Carica papaya is an important crop plant in many tropical and subtropical countries, where it is grown for its fruit as well as for medicinal purposes. The plant is also used in traditional medicine for the treatment of various ailments, such as digestive disorders, wounds, and skin diseases[8]

Chemical constituents of carica papaya:-

The separate part of papaya such as which are contain various chemical constituents.,which are given below.

1. Fruit- Protein, fat, fiber, carbohydrates, minerals: calcium, iron, vitamin C, thiamine, rivoflavin, niacin, and carotene, anino acid, citric acid and malic acids (green fruits), volatile compounds: benzylisothiocynate, cis and trans 2, 6-dimethyl-3,6 epoxy-7 octen-2-ol, alkaloids, carpaine.
2. Juice- N-butyric, n-hexanoic and n-octanoic acids, lipids; myristic acid, palmitic acid, stearic acid, linolenic acid, linoleic acid, oleic acid.
3. Seed- Fatty acids, crude protein, crude fibre, papaya oil, carpaine, caricin, glucotropacolin, and an anzyme myrosin.
4. Root- Carposides and an enzyme myrossin
5. Leaves- Alkaloids carpain, pseudocarpain, dehydrocarpaine I and II, choline, vitamine C and E, carposide.
6. Bark- Glucose, fructose, sucrose, xylitol, β-sitosterol
7. Latex- Papain, chemopapain, peptidase A and B, lysozymes papaya such as juice,fruit,root ,seed, bark ,latex contain various chemical constituents.[9]

Property of carica papaya:-

As with any potential treatment, it is always a good idea to speak with a healthcare professional before using papaya or any other natural remedy to address a health conccultures, the fruit of the papaya plant is the most recognizable feature. The fruit is a large, pear-shaped berry with a thin, smooth skin that ranges in color from green to yellow-orange when ripe. The interior of the fruit is filled with numerous small, black seeds embedded in a soft, juicy, orange-red flesh that has a sweet, musky flavor. The fruit is widely consumed raw or cooked in many tropical countries and is a significant source of nutrition and health benefits.

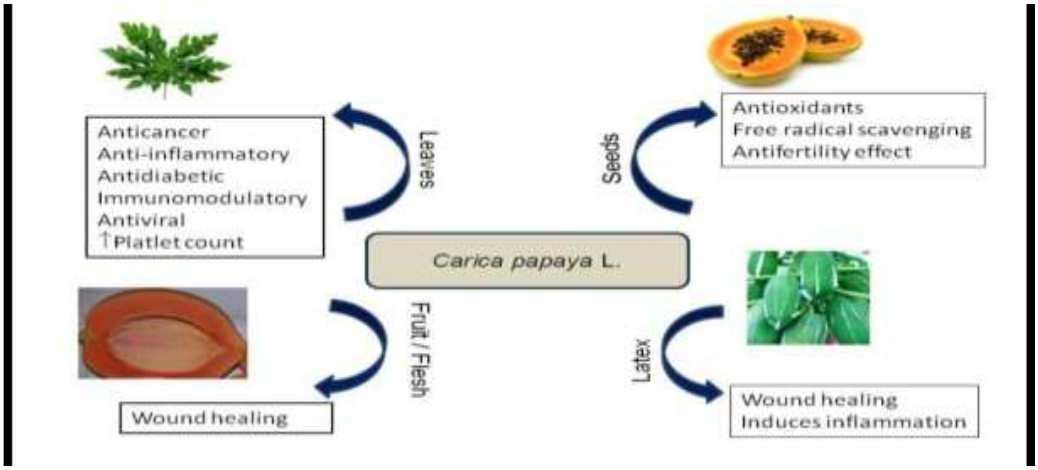

Fig.2:pharmacological effect of papaya

Phytoconstituents and Nutritional Value:-

Papaya contains a wide variety of phytochemicals, including vitamins (A, C, E, and K), minerals (calcium, potassium, magnesium, and iron), enzymes (papain and chymopapain), and secondary metabolites such as alkaloids, glycosides, saponins, and flavonoids. These phytoconstituents have various biological activities, including antioxidant, anticancer, anti-inflammatory, and antimicrobial effects.

In addition to phytochemicals, papaya is also a rich source of dietary fiber and low in calories, making it an ideal food for weight management. The fruit is also a good source of carbohydrates, particularly simple sugars such as fructose and glucose, and contains small amounts of protein and fat. Papaya is a rich source of

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carotenoids, particularly beta-carotene, which has been associated with a reduced risk of several chronic diseases, including cancer and heart disease.[10]

Medicinal and Pharmacological Properties:-

Papaya has been traditionally used in folk medicine to treat various ailments, including digestive disorders, wounds, and infections. Recent studies have provided evidence for several pharmacological properties of papaya, including its antimicrobial, antiparasitic, anticancer, and anti-inflammatory effects.

Antioxidant activity: -

Papaya contains high levels of antioxidants, which help to scavenge free radicals and prevent oxidative damage to cells. The antioxidant activity of papaya has been attributed to its high levels of vitamin C, carotenoids, and phenolic compounds.

Anticancer activity: -

Papaya extracts have been shown to possess potent anticancer effects against various cancer cell lines, including breast, colon, lung, and prostate cancer. The anticancer activity of papaya has been attributed to its ability to induce apoptosis (programmed cell death) and inhibit cell proliferation and angiogenesis.

Anti-inflammatory activity:-

Papaya contains several anti-inflammatory compounds, including flavonoids and phenolic acids, which have been shown to inhibit the production of pro-inflammatory cytokines and enzymes. Papaya extracts have been shown to possess anti-inflammatory effects in various animal models of inflammation, including rheumatoid arthritis and asthma.

Antimicrobial and antiparasitic activity:-

Papaya extracts have been shown to possess potent antimicrobial and antiparasitic effects against a wide range of pathogens, including bacteria, fungi, and protozoa. The antimicrobial activity of papaya has been attributed to its ability to disrupt the cell membrane and inhibit the growth of pathogens.

Anti-diabetic effects:-Papaya extracts have been shown to possess antidiabetic effects by reducing blood glucose levels and improving insulin sensitivity in animal models of diabetes. The antidiabetic effects of papaya have been attributed to its ability to enhance glucose uptake and glycogen synthesis in muscle and liver cells.[10]

Safety and efficacy of carica papaya:-

Carica papaya, also known as papaya, is a fruit that is commonly consumed in many parts of the world. While papaya has been traditionally used for medicinal purposes, there is limited scientific research on its safety and efficacy.

In terms of safety, papaya is generally considered safe when consumed in moderation as a food. However, some individuals may have an allergy to papaya or develop an allergic reaction after consuming it. Symptoms of an allergic reaction may include hives, itching, swelling, and difficulty breathing. In addition, the seeds of the papaya fruit should not be consumed in large quantities, as they contain a substance that can be toxic in high doses.

In terms of efficacy, papaya has been studied for its potential health benefits, including its anti-inflammatory, antioxidant, and immune-boosting properties. Some preliminary research suggests that papaya may have a positive effect on digestive health, including reducing inflammation in the gut and improving symptoms of constipation. Other studies have suggested that papaya may have anti-cancer properties and may help to lower cholesterol levels.[11]

Materials and Methods:

The primary outcome was the comparison of mortality between C. papaya and control. Secondary outcomes included platelet counts, hospitalization time, and adverse events. Search methods and identification of studies: A systematic search was performed in PubMed, Cochrane

Clinical Trial Registry, and Google Scholar [Appendix 1]. References of published articles were hand searched to find new studies exploring the efficacy and safety of C.papaya in dengue.[12]

Study selection:

Randomized controlled trials exploring the role of C. papaya compared with any comparator for patients of dengue and dengue shock syndrome were eligible for inclusion. Case reports and observational studies were not included in the analysis. Two review authors (Jaykaran Charan and Deepak Saxena) assessed titles and abstracts followed by full text (using predefined inclusion criteria) independently. For

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any disagreement decision of third author (Jagdish Prasad Goyal) was considered final.

Data collection and analysis Data extraction and management:

Two review authors (Jaykaran Charan and Deepak Saxena) extracted the data from included trials using a standardized data extraction form independently. Data were collected on study characteristics, patient characteristics, treatment characteristics, risk of bias using Cochrane risk of bias tool, and outcome data (mortality, platelet counts, hospitalization time, adverse events, etc.

Statistical analysis:-

Continuous data were summarized as mean difference (MD) and standardized MD (SMD) with 95% confidence interval (CI). The unit of MD was × 103/µl. In case of one clinical trial, the standard deviation of one follow- up parameter (increase in platelet count) was not given. On the basis of standard deviation of other parameter of same study and parameters of other studies, it was observed that there was not much difference in standard deviation between baseline and follow–up; hence, for that study (Yunita et al.), we considered follow- up standard deviation (SD) same as baseline SD during analysis results of Yunita et al. was given as subgroup to clarify the effect of this study on overall results. Dichotomous data was summarized as risk ratio (RR) with 95% CI. Random effect model was used for the analysis. Heterogeneity was using I
calculated values. We set predecided criteria for significant heterogeneity (I2 > 50%). We did not asses the publication bias as there were only four trials fulfilling the inclusion criteria, which were too less for assessing the publication bias. Review Manager version 5.3
software (Cochrane Collaboration) was used for analysis This review was performed as per the standards of Cochrane Collaboration and reported as per PRISMA standards.

Study charecteristics:-

There were total four trials included in the analysis.[13,17-19] Step by step method of inclusion and exclusion of studies is depicted in Figure 1. All studies were single-center randomized trials, except one which was multicentric. No trial was double-blind. Only one trial was placebo controlled trial, and in rest, standard treatments were considered as control. C. papaya was used by the different method in each trial. In one trial, it was used as leaf extract juice, in the second trial, it was used as leaf extract tablet and in remaining two trials, it was used as leaf extract capsule and leaf extract syrup, respectively. Follow-up was not same in all trials. It was 2 days, 5 days, 4 days, and 5 days, respectively.[13-15]

Assesment of Bias:- various parameters needed for the assessment of the risk of bias were not reported in these trials. As none of the trials was double-blinded; hence, there is a chance of bias, but at the same condition, endpoints such as platelet counts are objective parameters; hence, incorporation of the bias by open labeling of the trial may not significantly affect the result.[16]

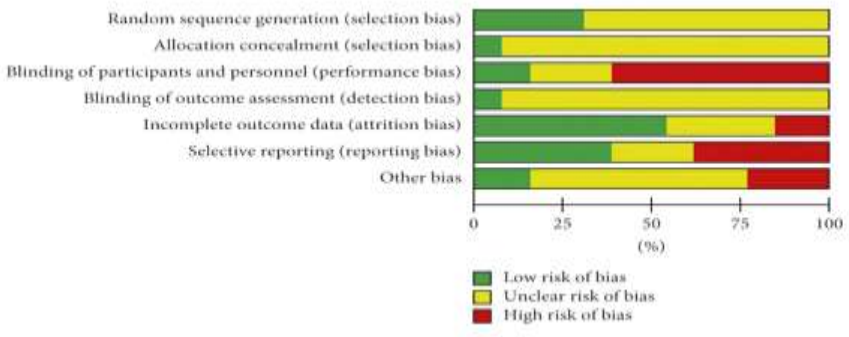

fig.3:Risk of bias graph

II. CONCULSION:-

Based on the meta-analysis,supplements with C.papaya leaf exctract in patient for treatment of dengue disease.

Based on the findings of the systematic review and meta-analysis, it can be concluded that the extract of C. papaya leaves plays a significant role in improving the platelet count in dengue patients. However, the magnitude of the rise in

platelet count may not be clinically significant, as indicated by the wider confidence interval. Although there is a statistically significant positive effect on the increase in platelet count, further investigation is needed to determine whether this rise has clinical significance. This can be achieved through the design of high-quality clinical trials, based on large sample sizes and incorporating measures to prevent bias.

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