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Role of Short Term Tamsulosin in Medical Management of Lower Ureteric Calculi in Today's Modern Era of Increasing Demand of Various Advancing Endo-Urological Procedures

By Aditya Avinash Yelikar

Abstract- Introduction: The choice of ideal method like MET or URS to treat lower ureteric calculi depends on the type of equipment available, type and size of stone, needs of the patient and skills of the surgeon. The smooth muscle relaxant drug tamsulosin (an α -adrenoceptor antagonist) is a possible agent, its use being termed medical expulsive therapy (MET). The disease spectrum in a developing country like ours is different from that of developed countries, mainly because of delay in diagnosis, delay in investigations and lack of awareness that tend to modify outcome in case of ureteral stones or for that matter any disease. More so, advanced interventional facilities in this part of the world are not easily available.

Methodology: A prospective study was thus planned to compare the tamsulosin group with a control group in our setup to evaluate the efficacy of tamsulosin for lower ureteric calculi expulsion within a few days without the need for hospitalisation, common endoscopic treatment or shock wave lithotripsy.

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Aditya Avinash Yelikar

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Methodology: A prospective study was thus planned to compare the tamsulosin group with a control group in our setup to evaluate the efficacy of tamsulosin for lower ureteric calculi expulsion within a few days without the need for hospitalisation, common endoscopic treatment or shock wave lithotripsy. The study included 600 subjects within age group of 20-50 years with solitary lower ureteric calculus of size 4mm-10mm.

Results: Use of tamsulosin in MET for lower ureteric calculi upto 9mm helps in expulsion of stone, reduces the need for hospital admission, reduces pain, reduces the need for oral analgesics and reduces the need for surgical intervention.

Conclusion: Tamsulosin therapy is not cost effective than watchful waiting but cost effective than surgical intervention.

I. INTRODUCTION

The choice of ideal method like MET or URS to treat lower ureteric calculi depends on the type of equipment available, type and size of stone, needs of the patient and skills of the surgeon [1]. The stone burden remains the primary factor in deciding the appropriate treatment for a patient with ureteric calculi [2].

Expectantly managed patients who develop recurrent pain, sepsis, or compromised renal function need drainage if necessary followed by stone clearance using endoscopy or extracorporeal shock wave lithotripsy [3].

The smooth muscle relaxant drug tamsulosin (an α -adrenoceptor antagonist) is a possible agent, its

use being termed medical expulsive therapy (MET)[4]. Meta-analyses of data from randomised controlled trials (RCTs) report a statistically significant benefit for tamsulosin over controls for the outcome of spontaneous stone passage [5,6].

Where a failed expectant treatment may well be complicated with hydro-nephrosis, deranged renal function or urosepsis. Interventional techniques are not always free of complications and failures. Most of the work of the efficacy of tamsulosin in lower ureteric calculi expulsion has been done in western affluent countries with variable results. The disease spectrum in a developing country like ours is different from that of developed countries, mainly because of delay in diagnosis, delay in investigations and lack of awareness that tend to modify outcome in case of ureteral stones or for that matter any disease. More so, advanced interventional facilities in this part of the world are not easily available. A prospective study was thus planned to compare the tamsulosin group with a control group in our setup to evaluate the efficacy of tamsulosin for lower ureteric calculi expulsion within a few days without the need for hospitalisation, common endoscopic treatment or shock wave lithotripsy.

II. METHODOLOGY

After taking clearance/permission from the ethical committee of our hospital we did a Prospective randomised control study from feb 2014 to feb 2017 including 600 subjects in age group of 20-50 years with unilateral ureteric calculi of size 4mm-10mm. Patients having acute renal failure, chronic renal failure, urinary tract infection, fever & who have recently undergone surgery for ureteric calculi were not included in the study. The study group was given cap Tamsulosin 0.4mg & tablet Dytor 10mg once daily for a maximum of 2 weeks or till the stone was passed (whichever was earlier). Analgesic (tablet diclofenac 100mg) was given as needed. The control group was given analgesic and diuretic tablets only for same period. During the study time an ultra sonography (KUB) was done on day 0 of starting tamsulosin treatment followed by on day 7, day 14 and day 17. Results were compared between the

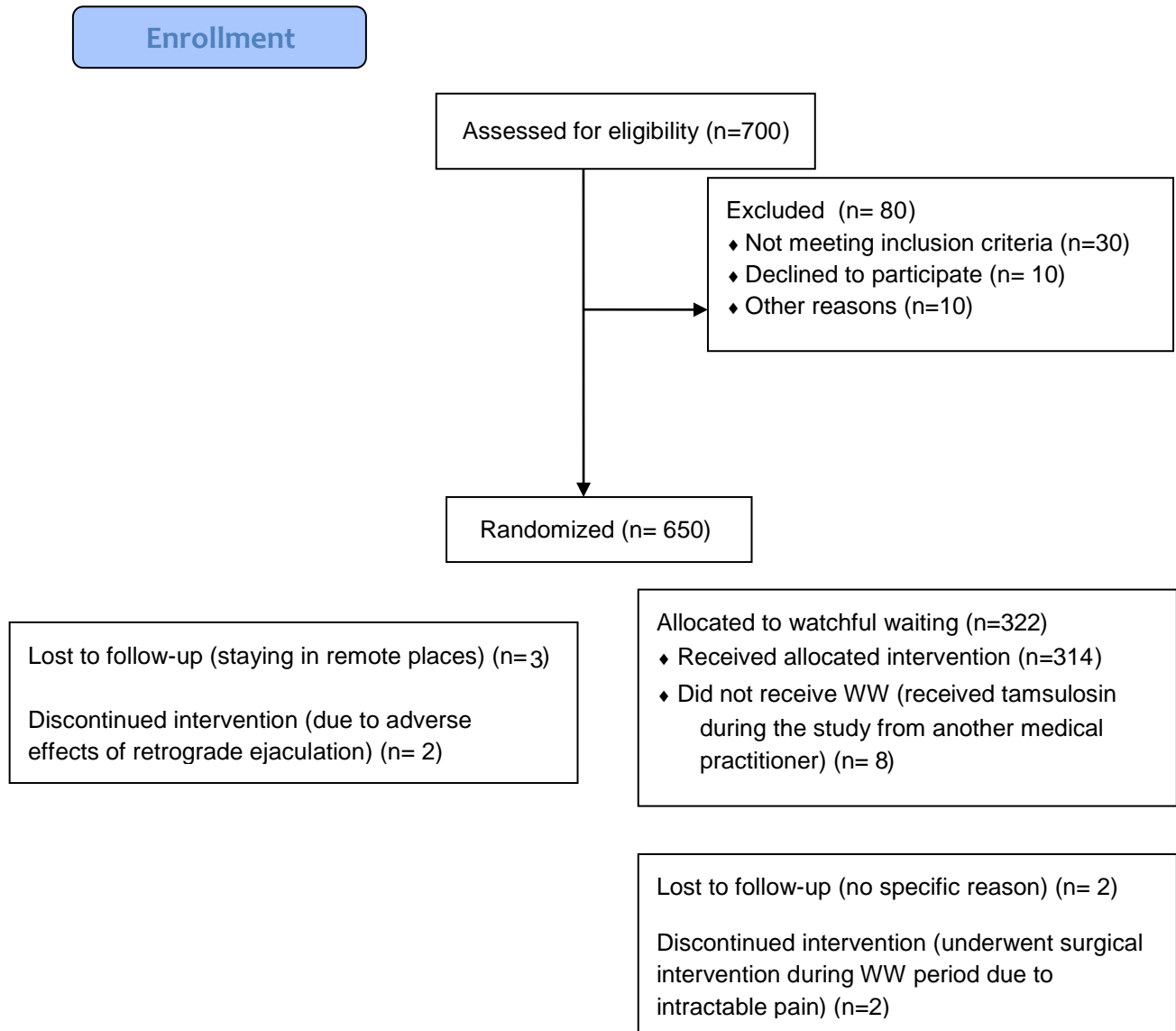
Author: e-mail: aditya.yelikar@gmail.com

study group and the control group in terms of stone passage rate, time taken to pass the stone, pain score during the treatment period, number & frequency of colic episodes and need for surgical intervention. Data was entered into MS word & Microsoft excel data sheet . Data was analysed using MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA). SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-Square test

was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t test (student's t test) was used as test of significance to identify the mean difference between two groups .p value < 0.05 was considered as statistically significant. Patients were randomized by using computer generated randomization from web site Randomization.com {<http://www.randomization.com>}. Double blinding was followed during the study period.

III. RESULTS & OBSERVATIONS

Consort Flow Diagram



All patients in our study were between the age group of 20-50 years. In our study the incidence of ureteric calculi was found to be more in males (81.44%) as compared to females (18.54%) .We found incidentally that more stones were on the right side (51.61%) as compared to the left side (48.38%) .No patient in group 1 had pain score in the range of 8-10 whereas 3.22% of

patients in group 2 had a pain score in the range of 8-10. 83.87% of stones in group 1 & 62.90% stones in group 2 passed out successfully. 17.74 % of patients in group 1 & 37.09% of patients in group 2 needed surgical intervention .However the need for surgical intervention for stone size up to 6mm was same in both the groups.

Table 1: Demographics of the study

		Mean age	Male	female	Left side stones	Right side stones	Mean stone size (USG)
Group	Tamsulosin	35.6 ± 8.5	230(74.2%)	80(25.8%)	165	145	7.5 ± 1.5 mm
	WW	35.9 ± 8.1	275(88.7%)	35(11.3%)	135	175	7.7 ± 1.4mm
p value		0.697	<0.001		0.016		0.132

p value of < 0.05 was considered significant

Table 2: Outcomes in the two groups

		Passed calculi in <14 days (%)	Not passed calculi	Mean no. of colic episodes	Mean pain score	Need for hospitalisation during treatment	Need for surgical intervention
groups	Tamsulosin	260 (83.87%)	50 (16.12%)	3 ± 1.7	4.1 ± 1.7	75	55 (17.74%)
	WW	195 (62.9%)	115 (37.09%)	4.2 ± 2.2	5.1 ± 1.8	135	115 (37.09%)
p value		<0.001	<0.001	< 0.001	< 0.001	<0.001	<0.001

NCCT was done in 70 (22.58%) cases in tamsulosin group and in 90 (29.03%) cases in WW group as USG could not detect any calculus. most of the stones detected by CT were of 5mm.

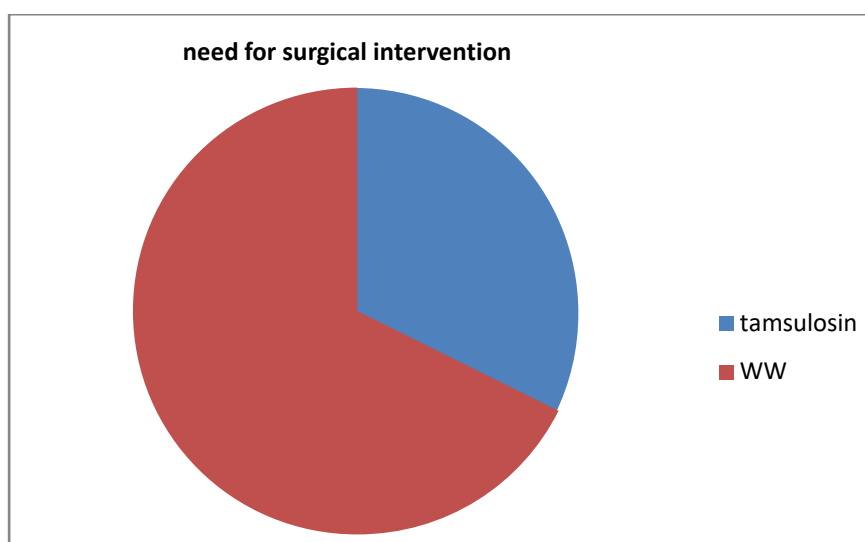


Figure: Pie diagram showing Surgical intervention comparison between two groups

IV. DISCUSSION

Treatment modalities for ureteral stones have greatly changed during the last 20 years, especially following the introduction of minimally invasive procedures such as extra-corporeal shock wave lithotripsy and uretero-renaloscopy. The advantage of the medical expulsive therapy is important, because the risks which are related to a surgical intervention are not trivial [7]. Studies have reported the overall complication rates after ureteroscopic lithotripsies to be 10–20%, with major complications such as ureteral perforations, avulsions and strictures occurring during 3–5% of the procedures [7]. Urinomas and sub capsular bleeds have been reported in 15–32% of the patients who are treated with shock wave lithotripsy [8]. Hollingsworth et al reported a 1.1% overall prevalence of MET use between 2000 and 2006 in emergency departments in

the USA, with a missed opportunity of sparing approximately 260,000 individuals annually from stone surgery[9]. 70% of urolithiasis are located in the lower third of the ureter. Determining factors for spontaneous passage of stones are their size, their configuration, and the smooth muscle activity of the ureters. In the transport of stones, the greatest obstacle is usually the terminal part of the ureters, mainly in the intramural 'detrusor tunnel'. Antagonists of the alpha-1-adrenergic receptor, in particular, inhibit basal tone and decrease peristaltic frequency and amplitude with the consequences of increased fluid transport and decreased intra-ureteral pressure; they also block the conduction of visceral referred pain to the central nervous system, acting on C-fibres or sympathetic postganglionic neurons [10,11,12,13]. Both the European (EAU) and American Urological Associations (AUA) outline the role of alpha-blockers as a viable

option in a select patient population who are comfortable with the approach and where there is no role for immediate surgical stone removal [14,15]. The role of alpha-blockers in MET has been well described [14-15]. The role of adrenergic receptors in the human ureter was first described in 1970 [16]. It was shown later, that the alpha-adrenergic receptors were classified into three different subtypes & the distribution in the human ureter was $\alpha1D > \alpha1A > \alpha1B$ [17]. It was also shown that the alpha-adrenergic receptor agonists had a stimulatory effect on the ureteral smooth muscle, whereas the beta-adrenergic receptor agonists had an inhibitory effect [18]. They prevent the uncoordinated muscle activity which is seen in renal colic, while maintaining ureteral peristalsis, which might facilitate a spontaneous stone passage [19]. The treatment effect on the expulsion rate was partially lost, as the sizes of the stones decreased, because of the high spontaneous expulsion rate of the small stones [2,20]. Our study included only solitary ureteral calculi & located in the distal one third of the ureter. Current best practice guidelines recommend alpha-blockers for the expulsion of distal ureteral stones. Meta-analyses have demonstrated that patients treated with alpha-blockers are more likely to pass stones with fewer episodes of colic [8,21]. Two recent randomized controlled studies by Al-Ansari et al [22] and Kaneko et al [23] validated the efficacy of tamsulosin for distal ureteral calculi. However, a randomized control trial by Yilmaz et al demonstrated that tamsulosin, terazosin, and doxazosin were equally effective in distal stone expulsion in comparison to the control group [24]. There is no role of tamsulosin or watchful waiting in stones of size ≥ 10 mm & Surgical intervention is the treatment of choice. In a recent study by Prof Robert Pickard et al [25] where they gave tamsulosin for 4 weeks they found that spontaneous stone passage, did not differ between groups. Comparing it with other studies we used tamsulosin maximum only for 2 weeks. In our study it was found that the use of tamsulosin increased the stone expulsion rate (83.87% in tamsulosin group compared to 62.9% in control group). We also found that the use of tamsulosin reduced pain and need for surgical intervention (17.74% in tamsulosin group compared to 37.09% in control group).

V. CONCLUSION

In our study incidence of ureteric calculi was found to be more in males in the age group of 31-40 years & on the right side. Use of tamsulosin in MET for lower ureteric calculi upto 9mm helps in expulsion of stone, reduces the need for hospital admission, reduces pain, reduces the need for oral analgesics and reduces the need for surgical intervention. There was no significant difference in number of days required for expulsion of stones between two groups. There was no

significant difference in mean size of stone passed in two groups. The possibility of expulsion of ureteric calculi spontaneously or with tamsulosin reduces as the stone size increases (maximum possibility with 5mm and minimum possibility with 9mm). There is no role of tamsulosin/watchful waiting in ureteric calculi of size ≥ 10 mm. Most common Complications associated with tamsulosin are giddiness, retrograde ejaculation. Tamsulosin therapy is not cost effective than watchful waiting but cost effective than surgical intervention. However our study had only two groups, one study group and one control group. Adding two more groups simultaneously, one with some other alpha blocker drug and one with no drugs given at all, may show us the exact efficacy of tamsulosin

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Study of Acute Toxicity of Phytopreparation Parodofit

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Keywords: acute toxicity, parodofit, liquid extract, dentistry, *salvia officinalis*, *matricariachamomilla*, *calendula officinalis*, *hypericum perforatum*.

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Study of Acute Toxicity of Phytopreparation Parodonfit

Zhuraeva Aziza Alisherovna ^α, S. A. Saidov ^σ & B.S. Tulyaganov ^ρ

Abstract- The object of the study is a liquid alcoholic extract under the code name "Parodonfit" - containing medicinal plants, such as *Salvia officinalis*, *Matricaria chamomilla*, *Calendula officinalis*, *Hypericum perforatum*. The chemical composition of this phytocomposition was previously studied. Moreover, alkaloids, flavonoids, saponins and tannins were found in the composition of the liquid extract. Given the traditional use of this phytocomposition in dentistry, it is of undoubted interest to develop a dental dosage form based on it for the treatment of diseases of the oral mucosa. The article presents the results of a study of acute toxicity of the Parodonfit liquid extract.

Keywords: acute toxicity, parodonfit, liquid extract, dentistry, *salvia officinalis*, *matricaria chamomilla*, *calendula officinalis*, *hypericum perforatum*.

I. RELEVANCE

The availability of modern affordable drugs is the basis for the treatment and prevention of the vast majority of diseases of modern man and an indicator of the social and economic development of society. The creation and implementation of new highly effective medicines (PM) based on plant materials growing in the regions of Uzbekistan is a priority for experimental scientists, technologists, doctors and public health authorities of the Republic of Uzbekistan. The development of drugs for dental practice is a very relevant area, since infectious and inflammatory periodontal diseases are common among the general population. According to the WHO, inflammatory periodontal diseases (gingivitis, stomatitis, glossitis, etc.) affect up to 95% of the world's adult population and up to 80% of children.

One of the most pressing problems of modern dentistry is inflammatory diseases of the oral mucosa, as well as gum bedsores (decubital ulcers), which are often formed when using removable dentures. Statistics from the World Health Organization indicate that symptoms of periodontitis are observed in 98% of adults and 76% of children. The disease begins as inflammation, continues with the formation of

periodontal (tooth-gingival) pockets and ends with the destruction of the cells in which the teeth are attached. Periodontitis is an inflammatory and destructive disease of the musculoskeletal system of the tooth, which occurs in almost 90% of the population. The development of drugs for dental practice is a very relevant area, since infectious and inflammatory periodontal diseases are common among the general population. The increased interest in medicinal plants, especially in the last decade, was the result of more frequent allergic reactions and complications after the use of antibiotics, hormones and other drugs. In contrast, medicinal plants rarely cause unwanted adverse reactions from the body, are non-toxic and well tolerated by patients regardless of age. Medicinal herbal remedies have high therapeutic efficacy and minimal toxicity [1].

Purpose of the study: The aim of this work is to study the acute toxicity of the Parodonfit liquid extract.

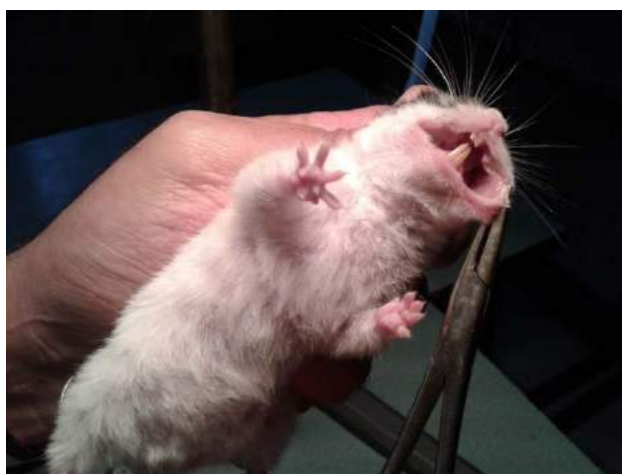
II. MATERIALS AND RESEARCH METHODS

The study of the acute toxicity of the test substance, with the Chlorophyllipt comparison drug, 1% alcohol solution in the first series of experiments was carried out according to the generally accepted method [1,2] on 42 white mice weighing 19-21 g of both sexes. The studied substance of the Parodonfit alcohol liquid extract in a ratio of 1:10 was administered to animals orally at a dose of 0.25; 0.5 and 0.75 ml per animal weight, which corresponds to 12.5 mg / kg, 25 mg / kg and 37.5 mg / kg. Control was animals that were orally injected with saline in an equivalent volume.

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Figure

Observation of the condition of the animals was carried out in vivarium conditions for 14 days. In this case, the general condition and behavior of the animals was taken into account. With the introduction of the substance at a dose of 12.5 mg / kg-25 mg / kg, no changes were noted. Animals were active, took water and food, reacted to external stimuli. While the introduction of 37.5 mg / kg contributed to a marked limitation of mobility, respiration became superficial and rapid. The observed changes lasted for 30-40 minutes,

then independently passed and the state of the animals returned to its original state. In this case, no pathological reactions in the behavior of animals were noted. They were active, there were no signs of intoxication and completely ate food. General behavior, coat color, mucous membranes, respiration, palpitations, locomotor activity, and death of mice were taken into account. The death of animals during the observation period (within 14 days) was not observed.

III. RESULTS AND DISCUSSION

Paradonfit		Chlorophyllipt 1% alcohol solution	
Dose mg / kg	The number of mice dead/ total	Dose mg / kg	The number of mice dead/ total
12,5	0/6	12,5	0/6
25	0/6	25	0/6
37,5	0/6	37,5	0/6

In the second series of experiments, in accordance with the methodological recommendations, acute toxicity was studied on Syrian sexually mature hamsters weighing 97-135 g by regularly treating the oral cavity of the Paradonfit liquid alcohol extract with a de-alcoholized evaporation method to 1/3 of the initial volume, followed by bringing water to the original amount 0.5-1.0 ml per animal. It is known that testing on Syrian hamsters is the most appropriate method for testing preclinical studies in dental practice [6]. To reproduce by irrigation, the studied alcoholic extract was introduced, which was prepared in advance in a dealcoholized form on the mucous membrane of the buccal space in an amount of 0.5-1.0 ml per animal.

Paradonfit	
Dose mg / kg	Number of hamsters dead / total
1 ml	0/3

Irrigation of the oral cavity was carried out daily for 10 days in vivarium conditions. The control group of animals was irrigated with 1 ml of tap water. Cages with animals were placed in separate rooms. The air

temperature was maintained in the range of 18-25 ° C, relative humidity - 30-70%. Acute toxicity was evaluated by changes in body weight and neuro-somatic indicators:

- General condition of the animal
- Behavior features
- The intensity and nature of motor activity
- The presence and nature of seizures
- Coordination of movement
- Reaction to tactile, pain, sound and light stimuli
- Frequency and depth of respiratory movements
- Condition of hair and skin

All manipulations with animals were carried out in accordance with the "International rules for working with laboratory animals" [4,5,7]. As a study of acute toxicity showed, the behavior of animals from the experimental group did not differ significantly from the control group. The condition of the coat and mucous membranes remained unchanged. During the experiment, no deaths were observed. Due to the above

parameters, there were no changes in laboratory animals.

IV. CONCLUSIONS

Thus, with a single oral administration, the Parodofit liquid alcohol extract in terms of acute toxicity compared to Chlorophyllipt 1% alcohol solution belongs to the class IV of relatively harmless substances [3], as well as during the irrigation of the oral mucosa on mature Syrian hamsters, the alcohol extract under study can be considered harmless.

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Healthcare Applications in IoT

By Md Sanju Islam, Fozilatoon Humaira & Dr. Fernaz Narin Nur

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Abstract- IoT is a blessing in the field of information and technology. It is developing and deploying day by day. It is working for our betterment in the section of home, environment, retail, security, factory, industry, agriculture, education, energy, healthcare and so on. In the healthcare section, it has applications, technologies, benefits and also challenges with the four-step architecture. As the world is aging with its uprising population, there is not enough opportunity for all to get healthcare. I think Health is the most expensive property one can own. So in the absence of sufficient and quality healthcare, IoT can manufacture the best utilization of its capacity to play a vital role in creating a better world for all of us. This paper represents the basic concept of IoT in the healthcare field.

Indexterms: *IoT, internet of things, healthcare applications.*

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Healthcare Applications in IoT

Md Sanju Islam ^α, Foziltoon Humaira ^ο & Dr. Fernaz Narin Nur ^ρ

Abstract- IoT is a blessing in the field of information and technology. It is developing and deploying day by day. It is working for our betterment in the section of home, environment, retail, security, factory, industry, agriculture, education, energy, healthcare and so on. In the healthcare section, it has applications, technologies, benefits and also challenges with the four-step architecture. As the world is aging with its uprising population, there is not enough opportunity for all to get healthcare. I think Health is the most expensive property one can own. So in the absence of sufficient and quality healthcare, IoT can manufacture the best utilization of its capacity to play a vital role in creating a better world for all of us. This paper represents the basic concept of IoT in the healthcare field.

Indexterms: IoT, internet of things, healthcare applications.

I. INTRODUCTION

IoT (Internet of Things) is a process of process that means all the electronic devices are connected with each other in a local area, forming a system. Further this system will connect to build up a bigger system. IoT is a concept or technology which aims to connect all the devices to the internet and help them communicate with each other using the internet as a medium. If we can connect any device to the internet it can be considered as an element for IoT. Some application areas of the Internet of Things are Home Automation, Healthcare, Agriculture, Transportation, Manufacturing, and Environment [1].

Before being on the era of IoT, a patient had to communicate with his doctor through visits, telephone, and text interactions. The doctors or hospitals could not monitor patient's health continuously and give advice accordingly, as there was no way to direct interactions all the time. But IoT has solved this problem by making remote monitoring possible in the healthcare field. It has the potential to keep the patient safe and healthy. It has also increased patient's engagement and satisfaction. As the interactions with the doctor has become more efficient, and trouble-free than earlier days. IoT is making a revolutionary transformation in the healthcare sector. The rest of the paper is arranged as follows: in Sec II, we have discussed the architecture, technologies of IoT based Healthcare system and in sec III, we have talked about the benefits and challenges of IoT in Healthcare sector. In sec IV, we have gone through

those above with the comparison table as a difference and with sec V, we have concluded the paper.

II. TECHNOLOGIES USED IN HEALTHCARE

IoT has a four-step architecture in Healthcare. All the stages are interconnected with each other:

Step 1(Devices): In the first step there will be devices (interconnected) which include sensors, monitors, camera systems etc. that will collect the data.

Step 2(Data Aggregation and Pre-processing): In the second step there will be analog data from the interconnected devices which need to be in total and translated into the digital form.

Step 3(Data Storage): If the data is in total and digital form, it will be moved to the data center or cloud.

Step 4(Data Analysis): Final data is examined with the records and further decisions are made [6].

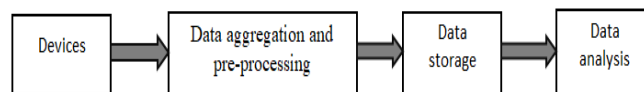


Fig. 1: Four-step architecture

There is a wide range of technologies in the field of healthcare in IoT. Advanced solutions have a deep strong effect on the fast growth of IoT. IoT healthcare solutions are supported by industrial science. Some technologies that can increase the IoT based healthcare services: Ultra-Low Power Sensing, IoT Processors, Cloud Computing, Grid Computing, Big Data, Communication Networks, and Wearable [2].

III. IOT BENEFITS AND CHALLENGES IN HEALTHCARE

By using IoT in the field of healthcare, we will be so much benefited that we can not describe in some words. But we can make an eye on some outstanding benefits of IoT in Healthcare. Such as Improved Treatment Outcomes, Cost Reduction, Faster Disease Diagnosis, Better Disease Management, Proactive Treatment, Improved Management of Drugs and Equipment, Enhanced Patient Experience, Simultaneous reporting and monitoring, End-to-end connectivity and affordability, Data assortment and analysis, Tracking and alerts, Remote medical assistance, Error Reduction [7] [6] [5]. Everything in the world has some difficulties

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in their way. As like everything IoT based healthcare services have various challenges that come from the sensors, communication networks and central servers. Some of the main challenges of IoT healthcare devices: Data security and privacy, Integration: multiple devices and protocols, Data overload and accuracy, cost, Energy Consumption of IoT Healthcare Device, Communication Network, Data Storage, and Continuous Monitoring [2] [5].

IV. RELATED WORKS

IoT is an element of the future internet. By reading some correspondent papers, we have got some ideas on IoT in the Healthcare sector. IoT applications in Healthcare can be in a single condition or clustered condition.

Single condition applications such as Glucose Level Sensing, Electrocardiogram Monitoring, Blood Pressure Monitoring, Oxygen Saturation Monitoring, Body Temperature Monitoring. And clustered condition applications such as: Rehabilitation System, Medication Management, Wheelchair Management, Imminent Healthcare, Smartphone Healthcare Solutions [3].

Table 1

Applications	Comparative Paper
Hearables, Ingestible sensors, Moodables, Computer vision technology, Healthcare charting	[5]
Glucose Level Sensing, Electrocardiogram Monitoring, Blood Pressure Monitoring, Oxygen Saturation Monitoring	[2]
Implantable Glucose Monitoring Systems, Activity Trackers During Cancer Treatment, Heart Monitors with Reporting, Medical Alert Systems, Ingestible Sensors, Medication Dispensers, Wireless Sensors, Trackable Inhalers, Wearables to Fight Depression, Connected Contact Lenses, Location Services	[8]
Interoperability/Data Management, Hospital Operations, Remote Patient Care	[9]

V. CONCLUSION

The rising technology Internet of Things is changing the lives by connecting limitless devices. In the near future IoT has a remarkable effect. There will be a net of IoT connecting worldwide devices. It will bring the nations closer. It will help to connect people and get information anytime and anywhere in the world. Health is one of the most important things for the human beings. We should monitor the health of the patients at all times. This paper puts the light on a survey of the healthcare applications regarding IoT. We are exploring IoT applications and here we also are working for additional insights. We also, studying the problems of many healthcare discussions.

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Study on the Development of Anti-Microbial Substitute Products Such as Fermented Feed and Chinese Medicine Feed

By Xiao Helang

Abstract- In this paper, the background of the development of anti-ban substitute products, the present situation and development prospect of anti-ban substitute products fermented feed, Chinese medicine feed and Chinese medicine feed additives, classification of fermented feed products, fermentation strains, processing technology and equipment requirements. The traditional Chinese medicine prescription medicine is the source of the traditional Chinese medicine feed additive, making the traditional Chinese medicine dregs fermented feed is the main way to utilize the traditional Chinese medicine dregs. This paper mainly introduces the source and treatment experiment of feed additive of Pulsatilla decoction for preventing and curing piglet diarrhea.

Keywords: *fermented feed, traditional chinese medicine feed and traditional chinese medicine feed additives, fermented strains, baitouweng soup feed additives, processing technology and equipment requirements.*

GJMR-B Classification: NLMC Code: QV 704



STUDY ON THE DEVELOPMENT OF ANTI-MICROBIAL SUBSTITUTE PRODUCTS SUCH AS FERMENTED FEED AND CHINESE MEDICINE FEED

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Keywords: fermented feed, traditional chinese medicine feed and traditional chinese medicine feed additives, fermented strains, baitouweng soup feed additives, processing technology and equipment requirements.

I. BACKGROUND OF THE DEVELOPMENT OF ANTI-BACTERIAL SUBSTITUTES SUCH AS FERMENTED FEED AND CHINESE MEDICINE FEED

China's Ministry of Agriculture and rural areas 'pilot Action Plan for reduction in the use of veterinary antimicrobials 2018 -- Prohibition of the use of pharmaceutical feed additives in feedstuffs by 2021 until the end of 2020, and formulated a series of "feed anti-resistance" regulations and "breeding end of anti-reduction, limit anti-" regulations. The harm of drug feed additives and misuse of antibiotics in breeding end has been recognized by people, but some people think that the comprehensive "feed prohibition" will cause the production level of breeding industry to drop, the

breeding cost will increase greatly, and the early stage of "feed prohibition" , on the contrary, the quantity of antibiotics used at the end of breeding increased, and "reducing resistance and limiting resistance at the end of breeding" became empty words. It is believed that anti-resistance will have an impact on animal husbandry: 1 Part of the survival of feed enterprises. Design of feed products. The implementation of the licensed veterinary surgeon system will be speeded up. 4. "Meat Without Resistance" becomes a new selling point. "TIKANG" products to meet the historical opportunities, this huge market space vacated by the "fermented feed, Chinese medicine feed, Chinese veterinary medicine, probiotics, " etc. , the future of these four categories of product manufacturers, operators or become the biggest beneficiaries, will usher in a spurt of growth. 6 The farm pays more attention to the hardware investment in the environment. Therefore, it is very important to develop and reserve alternative products such as fermented feed and traditional Chinese medicine feed. Only when the product of alternative medicine feed additive is mature, developed successfully and reaches a certain reserve amount, "breeding end to reduce resistance, limit resistance" will be achieved.

II. DEVELOPMENT OF FERMENTED FEED PRODUCTS

a) Concept and Product Classification of Fermented Feed

The concept of fermented feed: fermented feed refers to the full price feed or feed raw materials added beneficial bacteria for fermentation, beneficial microorganisms through their own metabolic activities, the anti-nutritional factors in plant, animal and mineral substances are decomposed and transformed into higher nutrient and non-toxic feed which is more easily taken up and digested by animals. In pig production, 5-10% is usually added to the Diet.

Fermented feed product classification: divided into three categories: 1 general raw material production of fermented feed: This category is very broad, because can be divided into conventional raw materials of products too many. This category is currently the most used in the field of aquaculture products. Corn meal, wheat bran, soybean meal, cotton meal, peanut meal,

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palm meal and other fermented feed. 2 Green Plants fermented feed: Green plants are mainly *Broussonetia Papyrifera*, *Opuntia Mori*, whole-plant corn, giant fungus grass, etc. . These plants are rich in nutritional value. After improvement, they are now planted in large quantities, especially *Broussonetia Papyrifera* and *Opuntia Mori*, is the national key support project, but this kind of plants do fermentation feed, there are certain limitations, that is, seasonal is strong, must concentrate harvesting and centralized processing, and more suitable for the combination of planting and breeding mode. 3 The fermented feed of the Offal of life: The most common is the fermented feed of bean dregs and distiller's grains, the low-cost raw materials, and the mixed fermented strains are used to make the fermented feed, in fact, it is a kind of recycling of resources, it is a kind of feedstuff with great development prospect.

b) Common Key Techniques of Fermented Feed

i. Fermentative Strains

Fermentation strains are *Bacillus subtilis*, *Bacillus licheniformis*, antimicrobial peptide *Bacillus*, *Lactobacillus acidophilus*, *Clostridium Butyricum*, *Saccharomyces Cerevisiae*, lactic acid bacteria and so on.

ii. Fermentation Substrate and Strain Selection

Singly or in combination. Is Advantageous to the metabolism product production, is advantageous in the digestion, the absorption, is advantageous in the digestion toxic, the harmful or the anti-nutrition material. Strain selection for fermentation substrate on different species of specific requirements: Control Mold Growth, production of antimicrobial substances, taste acid (not just acid), production of enzymes, high acid.

The main ingredients containing anti-nutritional factors are: 1 Cottonseed meal (cake): 1 cycloacrylic acid (egg white turns pink) and (2) Gossypol (free gossypol turns egg Yolk Olive). 2 Rapeseed meal (cake): 1) Sulfur Glucoside, which can be hydrolyzed into harmful substances thiocyanate and ISOTHIOCYANATE, which affect iodine metabolism; 2) myrosinase (eggs produce fishy smell). Flaxseed or flaxseed cake: flaxseed Gum, phytic acid, allergen, cyanogenic glycosides, trypsin inhibitors, anti-VB6 factors, etc. 3 CASSAVA DREGS: CYANOGENIC glucosides (including Linamarin and Stemonidin) can be converted to hydrocyanic acid. Potato (potato) dregs: GLYCOALKALOID (mainly containing Solanine), is an inhibitor of cholinesterase. 5 Sorghum: Tannin Reduces Palatability and Trypsin and alpha-amylase activity, forming a complex with VB12 to reduce VB12 absorption. 6 Palm Meal:-Mannan accounted for about 1 / 3 of the dry weight (NSP), dissolved in water to form a GEL, so that the contents of the digestive tract have a strong viscosity. Strain selection: spore-based special directional screening, strong specificity (for a certain or

several anti-nutritional factors), can degrade protein, fiber and other macromolecules, and produce a wealth of small and medium-sized new molecules. Rich in enzyme and acid production.

Crude fiber rich, medium protein residue bran and other raw materials: 1 Distiller's grains: crude fiber rich, low protein. Brewer's spent grains: good raw materials for dairy cattle, beef cattle and sheep, can be directly t, generally not recommended. 3 CASSAVA DREGS: CYANOGENIC glucoside (Linamarin and Stemonidin) can be converted into hydrocyanic acid. 4 Potato / POTATO DREGS: glycoalkaloid (Solanine), cholinesterase inhibitor. 5 Beet residue: Can Be fermented or not fermented feed pigs (10-25%), cattle, sheep 10-40%. Rice Bran: rich in crude fiber and very low in protein. 7 Rice Bran: rich in crude fiber, low protein, fat. 8 Bran: crude fiber is richer, protein is low, do not deal with commonly, can make water absorbent, ferment auxiliary material. 9 BEAN SKIN: The crude fiber is rich, the protein is low, palatability is poor. 10 Bean Straw: crude fiber is very rich, lignified, low protein. Strain selection: Spore, beneficial fungus mainly. Special Directional screening, strong specificity (degradation of cellulose), can produce acid, enzymes, vitamins, can add auxiliary fermentation agent.

Animal Slaughter and processing by-products: protein-rich, perishable, easily infectious pathogens, heat inactivated raw materials, there are: 1 Aquatic Processing Waste: Viscera, fish scales, skin, head, blood. LIVESTOCK AND POULTRY SLAUGHTER WASTE: Gastrointestinal contents, waste offal. Livestock and poultry blood, feathers: There are professional companies to deal with, raw materials for intense, high-value direction is the production of peptide products. LIVESTOCK AND POULTRY BONES: production of meat and bone meal, a professional company to deal with. 5 Dead Animals: Professional Companies, according to the law, made of meat and bone meal. Common Principles for processing: Hydrolysis by high pressure cooking or drying at 125°C. After cooking, fermentation, select spore, yeast, lactic acid and other complex bacteria plus enzyme hydrolysis.

iii. Fermentation Conditions and Process Control

Fermentation Mode: Solid State Fermentation (good fluidity). Semi-fluid fermentation (Porridge).

Fermentation Conditions: Temperature: 20-45 °C (different bacteria require different). MOISTURE: 20-85% (solid-state fermentation → semi-fluid). AEROBIC/ANAEROBIC: relating to the species used in the starter culture. TIME: 12-72H.

iv. Quality Control and Testing

Physics: Ph, color, taste, fluidity, etc. *BIOCHEMISTRY:* Fatty Acids, conventional nutrients (dry basis, fresh moisture), toxins, etc.

characteristics seriously affect the safety: Bacteria and improper storage, 1 week or so moldy.

v. *Technical And Equipment Requirements For Fermented Feed*

Process flow of fermented feed: weighing raw material according to formula Crushing → stirring inoculation: fermentative strain → adjust moisture content 50%-60%

→ sealed container → natural fermentation → inspection → fermented feed products.

Equipment Requirements: The equipment is fermentation tank, tank, or plastic bucket. The sealed container is used for all kinds of fermentation substrate fermentation.



Figure 1: Factory Production Line of fermenting feed tank

III. DEVELOPMENT OF TRADITIONAL CHINESE MEDICINE FEED PRODUCTS

a) *Traditional Chinese medicine prescription medicine and traditional Chinese medicine feed additive*

Traditional Chinese medicine mostly comes from nature, with little toxicity and side effect, low residue, reliable efficacy, safe use and high application value 1. Chinese medicine feed additive will replace antibiotic feed additive and play an important role in prevention and cure of animal epidemic disease. Chinese medicine is a treasure trove, such as Li Shizhen's Bencao Gangmu of the Qing Dynasty, 52 volumes, 1.9 million words, a collection of 1,892 Chinese herbs, 1,160 illustrations, and 11,096 prescriptions. Before modern times in China, human and animal plague occurred, that is to say, the Chinese herbal medicine decoction was used to eliminate the 2.

There are many prescription drugs of traditional Chinese medicine, the total effect of preventing and curing diseases is more than 85%. Due to the limited space of this article, the following are just 7 examples of traditional Chinese medicine prescription drug sources, formula plus or minus, treatment (anthelmintic) disease types.

1 Qingre Jiedu Representative Fang Yihuanglian Jiedu Tang Waitai Mi: huanglian 30g, huangqin 45g, huangbai 45g, Gardenia 30g. This prescription can be used for septicemia, Sepsis, dysentery, pneumonia and various acute diseases. Add Dandelion 30G, double flower 30g, folium Isatidis 35g, Radix isatidis 35g, agastache 25g, enhance the antibacterial and detoxification function. (2) the prescription of Xie Xia Representative Fang Yi da Cheng Qi Tang Shang Han Lun: Rhubarb 60 ~ 90g (lower back) , magnolia officinalis 30g, trifoliate trifoliate 30g, mirabilite 150 ~

300G (Chong). Witness fecal constipation knot, abdominal fullness, two will not pass, dry mouth, thick and dry moss, heavy pulse. The addition and subtraction of this prescription can treat constipation in pigs. 3 Yu Jin San (Yu Jin 35g, Huang Qin 35g, rhubarb 30g, coptis 30g, Phellodendron Amurense 30g, Terminalia Chebula 25g, Radix paeoniae alba 25g) to treat damp-heat diarrhea. When hot, should go to Terminalia Chebula, add honeysuckle 30g, forsythia 30g, to heat detoxification. 4 Xinliangjie, a representative of Fangyiqinqiao powder, was composed of 30g of Flos Lonicerae, 30g of Forsythia SUSPENSIA, 25g of semen sojae praeparatum, 25g of Platycodon Grandiflorum, 25g of Schizonepeta Tenuifolia, 30g of Lophatheri, 15g of mint, 20g of Niupanzi, 60g of asparagus root and 10g of licorice root. For the flu, bronchitis, pneumonia. Fever is even, add Gardenia, scutellaria, plaster to heat. 5 for all types of ASCITES junling powder. CODONOPSIS PILOSULA 30g, atractylodes macrocephala 30g, poria 30g, rhizoma alismatis 40g, Ramulus CINNAMOMI 25g, rhizoma atractylodis 15g, radix sophorae flavescentis 20g, cinnamon 20g, Ephedra 20g, Angelica 30g, dried Tangerine 30g. 6 Recipe of Leonurus Heterophyllus 60g, Angelica 45g, chuanxiong 30g, taoren 35g, Huangqi 30G, Dandelion 25g, honeysuckle 25g, liquorice 20g. 7 Insect repellent on behalf of Fang Yi areca powder. ARECA CATECHU 24g, cortex Melia Azedarach 18g, fructus AURANTII 15g, mirabilite (lower back) 15g, Crane Louse 9G, Rhubarb 9G, 12g. Deworming. This prescription is a relatively safe antiascaris agent. If the disease pig constitution is good, may add the thunder pill 9G, enhances drives the ascaris effect.

Traditional Chinese medicine feed additive is made into traditional Chinese medicine feed additive according to the proportion of each traditional Chinese medicine prescription medicine, take 3.3 made

Baitouweng soup feed additive as an example, not one example.

b) *Traditional Chinese Medicine fermented feed and traditional Chinese Medicine Dregs fermented feed*

Chinese Medicine fermented feed: refers to Chinese medicine slices and extracts by-products as substrate, under a certain temperature and humidity, through the inoculation of *SACCHAROMYCES cerevisiae*, *subtilis*, lactic acid bacteria and other strains and complex protease, cellulase, enzymes such as Xylanase make it undergo aerobic and anaerobic fermentation, fully expose the effective components of traditional Chinese medicine, improve its efficacy, and make the anti-nutritional factors in the feed decompose or transform, resulting in more animal feeding, digestion, absorption and higher nutrition, safe, non-toxic feed. Traditional Chinese medicine fermented feed can stimulate the animal's own non-Hapten function, play a disease treatment, disease prevention role.

Chinese Medicine Dregs fermented feed: millions of tons of Chinese medicine dregs are disposed of every year, resulting in huge waste of resources. Because the dregs also contain drug ingredients and nutrients, has not been absorbed by the human body, such as Ginseng, astragalus, Chuanxiong, tuckahoe dregs polysaccharide, glycosides, bases, amino acids, micronutrient remaining 20~30%. The traditional Chinese medicine dregs were collected and fermented to make the traditional Chinese medicine dregs fermented feed. Making fermented feed from Chinese medicinal dregs is the main way for the utilization of Chinese medicinal dregs.

c) *Feeding additives of Pulsatilla decoction as a substitute for medical feed additives in the treatment of piglet diarrhea*

Drug feed additives (products) were previously designed for the prevention and treatment of piglet diarrhea, one is high zinc feed additives (the maximum zinc content in the formulated feed for piglets is 110mg / kg, and the treatment of diarrhea in piglets is increased to 1600mg / kg by zinc oxide or basic zinc chloride), the other is antibiotic feed additives, there are Aureomycin Premix, oxytetracycline calcium premix, bacitracin zinc premix and so on.

"Baitouweng decoction" was first published in the treatise on Febrile Diseases. Jue Yin Chapter, it is composed of 4 herbs: Pulsatilla Chinensis, Cortex Phellodendri, Rhizoma Coptidis and CORTEX Fraxini. Pulsatilla Chinensis can clear away heat and toxin, cool blood and treat dysentery. The combination of the four herbs can clear away heat and detoxication, cool blood and stop dysentery. 3, the prescription: Pulsatilla Chinensis 60g, cortex phellodendri 45g, cortex fraxini 45g, Rhizoma Coptidis 45g, treat the damp-heat diarrhea caused by large intestine heat toxin injury in

blood. Its main components are alkaloids, coumarins, saponins. The combination of Baitouweng decoction and antipyretic and antidotal drugs can decrease the endotoxin of *E. Coli*, increase the blood viscosity, shorten the prothrombin time and increase the Hematocrit 4. Pulsatilla contains triterpene saponins, triterpene acids, Lignans, pulsatilla Chinensis, pulsatilla Chinensis, pulsatilla Chinensis, pulsatilla Chinensis, pulsatilla Chinensis, pulsatilla Chinensis, pulsatilla Chinensis, Dauconin and Glycoprotein. The different extracts of Pulsatilla Chinensis and the composition of Pulsatilla Chinensis decoction have bacteriostatic effect on *Staphylococcus Aureus*, *Escherichia Coli*, *Pseudomonas Aeruginosa* and paratyphoid *Bacillus* 6.

According to the formula of Baitouweng decoction: Baitouweng 60g, cortex phellodendri 45g, cortex fraxini 45g, Rhizoma Coptidis 45g, semen Plantaginis 35g, tuckahoe 25g, rhizoma atractylodis 25g each, 280g subtotal. Baitouweng Soup Chinese medicine feed additive was confected by percentage: Baitouweng 21.4% (6028000.214,0214100% 21.4%, same as below), cortex phellodendri 16.1%, cortex FRAXINI 16.1%, rhizoma COPTIDIS 16.1%, rhizoma plantaginis 12.5%, poria 8.9%, RHIZOMA ATRACTYLODIS 8.9%. Used to replace antibiotics, antibiotics feed additives and PULSATILLA decoction prescription medicine.

How effective are pulsatilla decoction and Pulsatilla decoction feed additives in treating piglet diarrhea? Can baitouweng soup feed additive replace antibiotic, antibiotic feed additive and Baitouweng Soup prescription drug? Therefore, the author designed and carried out a test to treat piglet diarrhea, using Ofloxacin injection treatment group as control group, Baitouweng decoction prescription drug treatment group as group I, 15% Baitouweng decoction feed additive group as Group II, 10% baitouwengtang feed additive group III was used to treat diarrhea piglets in order to confirm whether Chinese medicine feed additive can replace antibiotics and Chinese medicine prescription. From December 2, 2018 to February 27, 2019, 50 pigs in each group were tested in Dongkou Jiajing Agriculture and Animal Husbandry Co., Ltd. (7000 pig farms). The results are shown in Table 1.

Table 1: Therapeutic effect of ofloxacin, pulsatilla Chinensis and Pulsatilla Chinensis on piglet diarrhea in Dongkou County

	Control Group	Group I	Group II	Group III
Treatment head count	50	50	50	50
Number of heals	47	46	45	40
Cure rate%	94.0	92.0	90.0	80.0
Average number of days cured	2.8	3.3	3.6	4.5
Drug expenditure (per head / Yuan)	12.4	11.6	10.9	9.8

The results showed that the cure rate of Group II was 90.0% , and the average cure time was 3.6 days, the cure rate of Group II was 94.0% , the average cure time was 2.8 days, the cure rate of group I was 92.0% , the average cure time was 3.3 days, the difference was not significant (P & GT; 0.05) , the results showed that 15% BAITOUWENG decoction could replace the prescription of Ofloxacin and Baitouweng decoction, the cure rate of Group II was 80.0% and the average cure time was 4.5 days, the difference was significant (P & Lt; 0.05) , the results showed that the 10% Baitouweng decoction with feed additive was too little to reach the prescription dosage of Baitouweng decoction, which affected the therapeutic effect. Therefore, 10% baitouweng soup feed additives can only be used as a preventive amount, treatment of 15% to 20% (add 15-20%), in order to achieve the Baitouweng soup prescription drug treatment effect.

IV. CONCLUSION

It is still in the research and development stage at present. Although there are many commercial products on the market, because of the late start, new subjects, the theoretical research, feeding experiment and practical application of fermented feed should be strengthened. Therefore, with the advent of the era of prohibition and resistance, agricultural colleges and universities have strengthened the education of fermented feed, Chinese veterinary medicine and Chinese medicine feed for undergraduates, and strengthened the on-the-job training for livestock workers, vocational Training and knowledge updating education of fermented feed and traditional Chinese medicine feed are very important.

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In-Vitro Antioxidant, Anti-Inflammatory and Anti-Microbial Activity of *Carica Papaya* Seeds

By Pooja G. Singh, Madhu S. B, Shailasreesekhar, Gopenath TS,
Kanthesh M. Basalingappa & Dr. Sushma BV

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Keywords: *carica papaya* L., seed extracts, phytochemical analysis, antioxidant, lipoxygenase inhibition, antimicrobial activity.

GJMR-B Classification: NLMC Code: QV 738



Strictly as per the compliance and regulations of:



In Vitro Antioxidant, Anti-Inflammatory and Anti-Microbial Activity of *Carica Papaya* Seeds

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& Dr. Sushma BV [§]

Abstract- Papaya seeds are reported to have higher therapeutic potential in comparison to the fruits in which they reside. Thus, the present in-vitro study aimed to evaluate and compare the anti-oxidant, anti-inflammatory and anti-microbial effect of seed extracts on *Carica papaya* L. (Caricaceae). The bioactive form the seeds were sequentially fractionated with hexane, chloroform, diethyl ether, and methanol in the increasing order of polarity. Total phenolic and flavonoid contents were estimated. These extracts were assessed for an antioxidant property by 1, 1-diphenyl-2-picryl-hydroxyl (DPPH) method and reducing power assay was carried out using the FeCl₃ method. Inhibition of 15-lipoxygenase (LOX) by these extracts at 5 - 25µg to assess anti-inflammatory capacity was studied.

Antibacterial activity against some human pathogenic bacteria was tested by agar disk diffusion method. Among all the organic solvent extracts, methanolic extracts exhibited good antioxidant and antibacterial activity. Methanolic extract with an IC₅₀ value of 48mg for LOX inhibition is reported. The extracts showed inhibition of human pathogenic bacteria in the order: *Escherichia coli* > *Pseudomonas vulgaris* > *Klebsiella pneumonia*. Significant and positive linear correlations were found between total antioxidant capacities and phenolic contents indicating that phenolics were the dominant antioxidant constituents in tested seeds. Methanol extracts of *C. papaya* were subjected to LC-MS metabolite profiling. The LC-MS analysis identified 6 metabolites *p*-hydroxybenzoic acid, salicylic acid, hyperoxide, gental alcohol, triallyl glucose, kaempferolhexoside as the main constituents for the first time from this seed extract. Our study demonstrated that the selected papaya seeds have good antioxidant, anti-inflammatory, and antibacterial properties.

Keywords: *carica papaya* L., seed extracts, phytochemical analysis, antioxidant, lipoxygenase inhibition, antimicrobial activity.

I. INTRODUCTION

Papaya (*Carica papaya* L.) is a member of the family Caricaceae. This plant family has four genera including Jarilla, Cylicomorpha, Cylicomorpha, and Carica. *Carica papaya* L. is common papaya and extensively grown over the world. The plant is herbaceous, soft tissue and fast-growing. Common names include papaya, papaw or pawpaw, Papeete (Pakistan), paper (French), Tenenbaum (German), chose (Spanish), mamao, mamoeiro (Portuguese), mugu (Chinese) and Malakal (Thailand). Papaya is a fruit plant with a soft stem, commonly and erroneously referred to as a tree. The papaya seeds contain balance-nutrients which consist of protein (24.3%), fatty oil (25.3%) and total carbohydrate (32.5 %). Although it contains a significantly high level of unsaturated fatty acids, papaya seeds seem not to be good oil seeds. Papaya seeds are used generally as an anti-parasitic agent by humans' plant is properly a large herb growing at the rate of 1.8-3 m in the first year and reaching 6-9 m in height[1]. The lower trunk is conspicuously scarred where leaves and fruit are borne. In some parts of the world, papaya leaves are made into tea as a treatment for malaria, dengue but the mechanism is to be scientifically proven. Papaya contains about 6% of the level of beta carotene. Excessive consumption of papaya may cause carotenemia, the yellowing of soles and palms[15]. Papaya releases a latex fluid when not ripe, possibly causing irritation and an allergic reaction in some people.

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Figure 1: Papaya Fruits with Seeds

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a) Chemicals and Reagents

Linoleic acid, 1, 1-diphenyl-2-picrylhydrazyl (DPPH), catechin were purchased from SIGMA ALDRICH (USA, MO). Sodium bicarbonate, 15-lipoxygenase, aluminum chloride, gallic acid, ascorbic acid, trichloroacetic acid (TCA), potassium ferricyanide, ferric chloride, folic-ciocalteu (FC) potassium buffer, borate buffer, nutrient agar, peptone, beef extract, hexane, chloroform, diethyl ether, methanol, borate salt, sodium dihydrogen phosphate, disodium hydrogen phosphate were laboratory chemicals.

b) Processing of Plant Samples

Carica papaya fruits were collected from Mysore district, Karnataka, India. The pawpaw fruits were washed in tap water and then rinsed in sterile distilled water. The seeds were removed and shade-dried for about a week and were crushed using liquid nitrogen using mortar and pestle. Seeds were ground into a coarse powder. Fractionation of bioactive compounds was carried out using a solvent to increase the polarity of the solvents like hexane, chloroform, diethyl ether and methanol for 48 h in dark with constant stirring at room temperature. After each fractionation, the respective solvents were carefully filtered using a muslin cloth to prevent contamination by seed residue. The clear extract was air-dried to get a fine paste. The extract was weighed and stored at 4°C in dark until further analysis.

c) Extraction Of Plant Material

About 25 g of coarsely powdered papaya seeds were weighed and suspended into 200mL of the solvent (hexane, chloroform, diethyl ether, and methanol) based on the increasing order of polarity. The extraction was

carried out at room temperature for 48 h using rotatory shaker at 30°C 60 rpm for 48 h. The extracts were first filtered with a clean muslin cloth and then suction filtered using flash operator at 44°C 160 rpm and finally dried it in glass Petri dishes at RT. The final drying process was carried out using by collecting the filtrates in the Eppendorf tube and dried in speed vacuum for 3 h at 40°C and the extracts were stored in dark at 4°C till further use.

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Qualitative Analysis of Saponins and Tannins

a) A Test for Saponins

About 0.1 g of methanolic extract was diluted in 1ml of methanol. Extract (0.5 mL) was taken in a test tube and solubilized using 4.5mL of distilled water[2]. The formation of stable foam indicated the presence of Saponins.

b) A Test for Tannins

About 0.1 g of methanolic extract was diluted in 1ml of methanol. Extract (0.5 mL) was taken in a test tube and mixed with 10mL distilled water and ferric chloride reagent (3 drops,) added to the filtrate. A blue-black green precipitate confirmed the presence of Gallic tannins or catechol tannins[2].

c) Determination of Total Phenolics

The total phenolic content was estimated using the Folin-Ciocalteu (FC) calorimetric method. Gallic acid (20-100mg) standard was prepared. Extract (0.1 g) was weighed and diluted to make 100mg in 100mL. The extract (20-100mL) reacted with FC reagent (250mL) and was incubated at RT for 5min[3]. The reaction was neutralized with saturated sodium bicarbonate (1.5mL,

20%) that was added to the mixture and allowed to stand for 1 h[6]. The absorbance of the resulting blue color was measured at 765 nm (BECKMAN COULTER, DU 730 LIFE SCIENCE UV/VISIBLE SPECTROPHOTOMETER). Total phenolics content in the methanol extract of seeds was quantified by the calibration curve obtained from measuring the absorbance of known concentrations of gallic acid standard. The total phenolic contents were expressed as gallic acid equivalence (GAE) in μg .

d) Determination of Total Flavonoids

The total flavonoid content was determined by the aluminum chloride colorimetric method[5]. In brief, 10- 50 mL of extract were made up to 1mL with methanol, mixed with 4mL of distilled water and then 0.3mL of 5% NaNO_2 solution. AlCl_3 (0.3mL of 10%) solution was added after 5min of incubation and the mixture could stand for 6min. Then, 2mL of 1 mol/L NaOH solution was added, and the final volume of the mixture was brought to 10 mL with double-distilled water. The mixture could stand for 15min, and absorbance was measured at 510nm. The total flavonoid content was calculated from a calibration curve, and the result was expressed as μg catechin equivalent per g dry weight[9].

e) Antioxidant Activity

i. DPPH radical scavenging assay

The free radical scavenging property of the methanol extracts of papaya seeds was determined by the DPPH method. An aliquot of the extract was dissolved in a solvent and was plated out in duplicate in a 96- well microtiter plate. The DPPH radical solution (50mM; 2.9mg in 25mLmethanol) was added to alternating columns of the test samples and methanol was used as control. The percent of decolorization was recorded spectrophotometrically at 517nm using the Thermo Scientific Varioskan Flash Microtiter Plate Reader. The reaction for scavenging DPPH radical was in dark and the absorbance was recorded at 517 nm (Spectra Max, Molecular devices). Percent radical scavenging activity was determined by comparing with a solvent added as a control. The IC_{50} values were determined, which denote the Concentration of extracts required to scavenge 50% DPPH radicals[4]. Ascorbic acid (0.1 g in 5mL) was used as positive control at least three independent tests were performed for each sample. Solvent extracts of hexane, diethyl ether and methanol were tested[6]. Percent scavenging effect was determined by the following equation: % inhibition = $[(\text{Absorbance of control} - \text{Absorbance of the test sample})/\text{Absorbance of control}] \times 100$ [7].

f) Reducing Power Assay

This estimation of reducing power was carried for papaya seeds with slight modifications. Test solution (0.1mL, 1mg/mL) was mixed with equal volume of

phosphate buffer (0.2M, pH 6.6) and potassium ferricyanide (2.5mL, 1%) and was incubated at 50°C for 20 min. Trichloroacetic acid (TCA; 10%, 2.5mL) was added to the mixture, which was then centrifuged at 3000 rpm for 5 min. After centrifugation, the supernatant solution (1.5mL) was taken in a test tube and was mixed with an equal volume of distilled water and ferric chloride (0.5mL, 0.1%). Ascorbic acid was used as a standard and phosphate buffer was used as a blank solution. Absorbance was measured at 700nm (Beckman-Colter, Du 730 Life Science Uv/Visible Spectrophotometer). Increased absorbance of the reaction mixture indicates stronger reducing power[8].

g) Anti-Inflammatory Activity

i. Lipoxygenase assay (LOX)

Carica papaya seeds were extracted and solubilized in methanol and tested for in vitro anti-inflammatory activity spectrophotometric assay for determination of LOX activity for papaya seed. Weight of empty Eppendorf tube was noted and 5mg of methanol extract was taken in empty Eppendorf tube extract was diluted using 1ml of methanol and shaken well. 15-LOX (5mg) activity with linolenic acid(0.2mM) in borate buffer (0.2M, pH 9.0) was carried out methanol extract (5, 10, 15, 20ml). The inhibition of LOX by the extracts was recorded by the time scan method at 234 nm[10]. Ascorbic acid inhibiting LOX was as recorded at 234nm using UV- Visible Spectrophotometer (Beckman-Coulter, Du 730 Life Science Uv/ Visible Spectrophotometer). The inhibitory effect of the extract was expressed as % of enzyme activity inhibition (IC_{50}) value indicating the concentration required to inhibit 50% LOX activity[14]. It was calculated using the formula % of inhibition = $[(\text{initial activity} - \text{inhibitor activity})/\text{initial activity}] \times 100$.

h) Antibacterial Activity

i. Determination of Antibacterial Activity

Antibacterial activity of methanolic extracts (1, 2.5, 5 10 μL) of papaya seeds was determined by the disc diffusion method. The bacterial samples tested were *Escherichiacoli*, *Klebsiellapneumonia*, and *Pseudomonasvulgaris*. The media was prepared using peptone (3.75g), beef extract (2.25g), agar (15g) and distilled water (750mL). The contents were transferred to a flask and were plugged with cotton and wrapped using brown paper. Glass Petri plates were washed thoroughly rinsed with methanol and autoclaved at 121°C for 15min for complete sterilization[11]. The agar solution could cool, and 15 mL was poured into sterile glass Petri plates. The plates could set and then incubated at 37°C overnight. Colonies were picked from plates and used as inoculums of test organisms. The plates were incubated at 37°C overnight. Disc of Whatman No.1 filter paper was sterilized by heating in an oven for 30 min at 80°C[12]. Agar plates were inoculated with each organism and after 5 min, 6 filter paper discs,

impregnated with 5mL of the concentrated extracts, streptomycin (0.5mg/mL) were transferred onto the agar plates using sterile forceps. The plates were then incubated at 37°C overnight. The effectiveness of the extract as an antibiotic against the test organism was determined by measuring the diameter of the zone of inhibition.

ii. LC-MS ANALYSIS

For the qualitative analysis of the metabolites were analyzed by Synapt G2 (UPLC separations with Quant of) according to the manufacturer's protocol. The nebulizer pressure was 60 psi and the nitrogen flow rate 10 L/min at a drying temperature of 350°C. The methanol seed extract was filtered (0.2-micron syringe filters, Millipore, U.S.A) and an aliquot (5 µl) was injected into the system. The mass spectra were acquired from m/z 100-1000 in negative ionization mode. Helium was used as the collision gas for the fragmentation of the isolated compounds in the ion trap[13]. The detection conditions were as follows: capillary voltage, 3500 V; skimmer voltage, -40 V; cap exit voltage, -158.5 V; Oct 1 DC, -12 V; Oct 2 DC, -2.45 V; trap drive level, 45.0; Oct RF, 150 Vpp; Lens 1, 5.0 V; Lens 2, 60 V.

Y P

Carica papaya seed extract was prepared using four different solvents (hexane, chloroform, diethyl ether, and methanol) for the screening of bioactive capacity. The analysis was performed using a generally accepted

laboratory technique for qualitative determinations. Saponins test performed showed a positive result for hexane, diethyl ether and methanol whereas negative for chloroform. The tannins test conducted showed a positive result for hexane and methanol whereas negative results for chloroform and diethyl ether extracts. Thus methanol extract of *C.papaya* seeds contains saponins, tannin compounds. The importance of saponins and tannins in various antibiotics for treating common pathogenic strains has been reported[16].

Table 1: Phytochemical screening of methanolic extract of papaya seeds

Bioactives	Hexane	Chloroform	Diethyl Ether	Methanol
Tanins	+	-	-	+
Saponin	+	-	+	+

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P

Quantitative Analysis of Total Phenols and Flavonoids

a) Total Phenolic Content

Total phenolic contents of the methanolic fractions of the seed of *C. papaya* were determined by using the Folin-Ciocalteu reagent and were expressed as gallic acid equivalents (GAE) per gram of seed extract. The total phenolic contents were 147µg for methanol extract of papaya seeds.

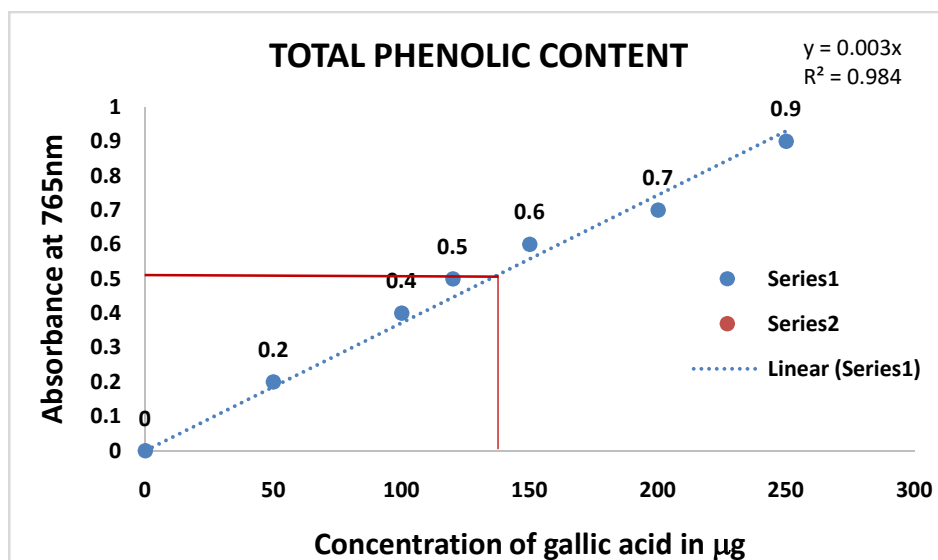


Figure 2: Total phenol content of 147µg gallic acid equivalent (GAE) was recorded using standard prepared by gallic acid

b) Total Flavonoid Content

Flavonoids are secondary metabolites, the antioxidant activity of which is dependent on the presence of free -OH group, especially 3-OH. The total flavonoid content was 100mg for methanol extract of

papaya seeds. As this is the report on the antioxidant activity of *C. papaya* through phytochemical analysis, identification of the active phenolic and flavonoid compounds was attempted.

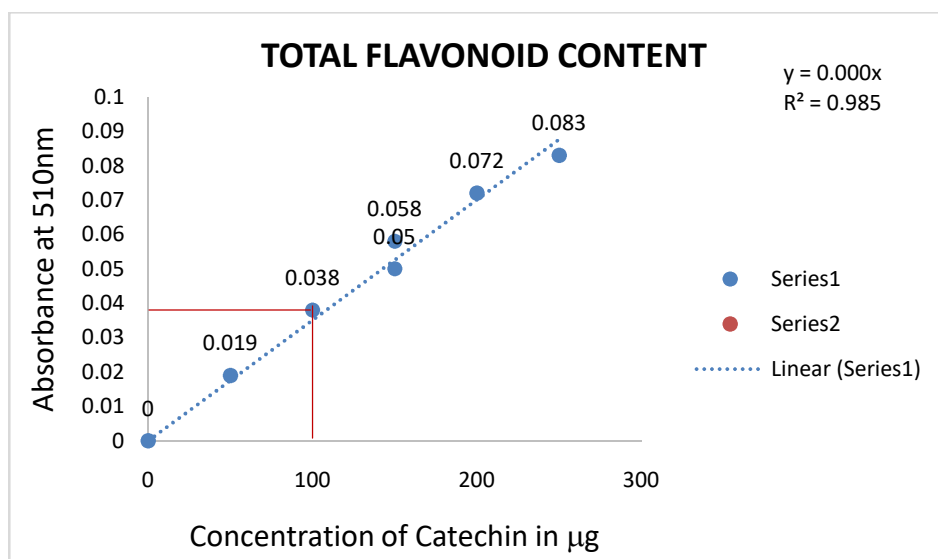


Figure 3: Total flavonoid content of 100 μg and estimated GAE recorded using Standard prepared by catechin

c) Antioxidant Activity

DPPH radical scavenging activity (%) can be calculated by using the formula as mentioned previously. Based on the results obtained, a graph also was prepared. The graph showed the percentage of radical scavenging activity of methanolic extracts at different concentrations with 50% of DPPH scavenging activity at 32mg.

Similarly, DPPH scavenging capacity for hexane, chloroform and diethyl ether for various extract concentration is reported. A comparison of the ability of various concentrations of seed-extract of hexane and diethyl ether with methanol extract indicated their limited DPPH scavenging capacity.

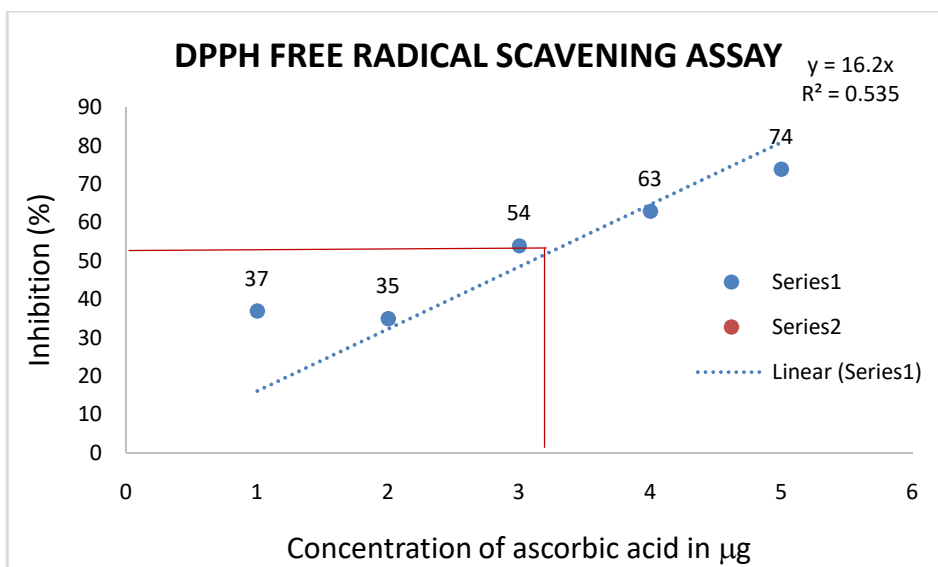


Figure 4: DPPH scavenging capacity of methanolic seed extract

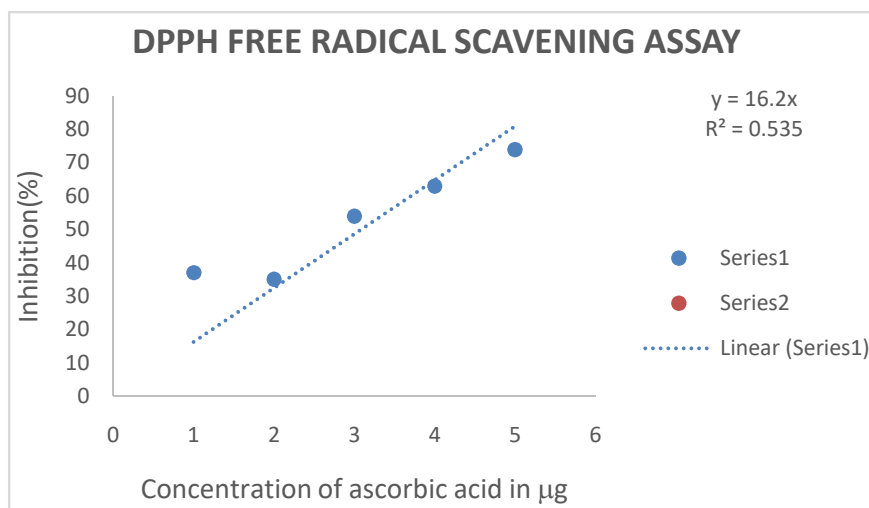


Figure 5: DPPH scavenging capacity of hexane seed extract

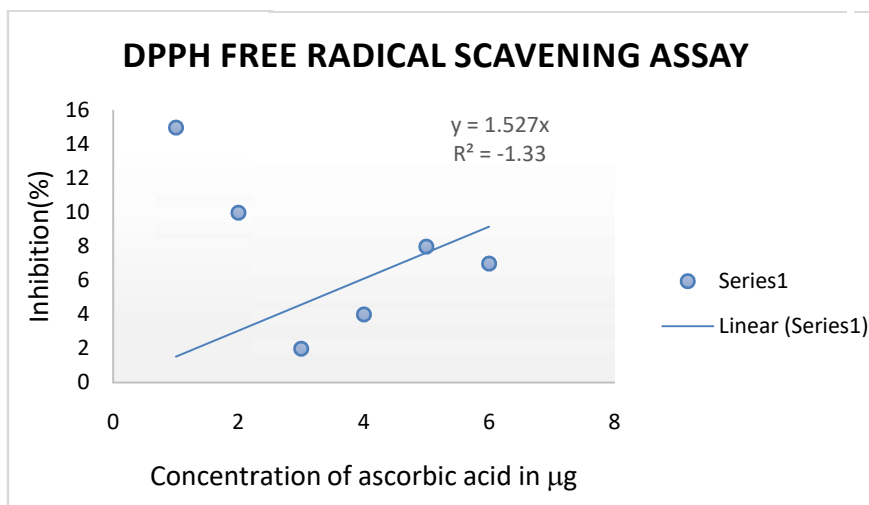


Figure 6: DPPH scavenging capacity of diethyl ether seed extract

The reducing capacity of the papaya seed methanol extracts was compared to standard ascorbic acid. An increase in absorbance at 700 nm indicates the

reducing power of the extracts. The graph shows the concentration of methanol extract to scavenge 50% of added reducing chemical.

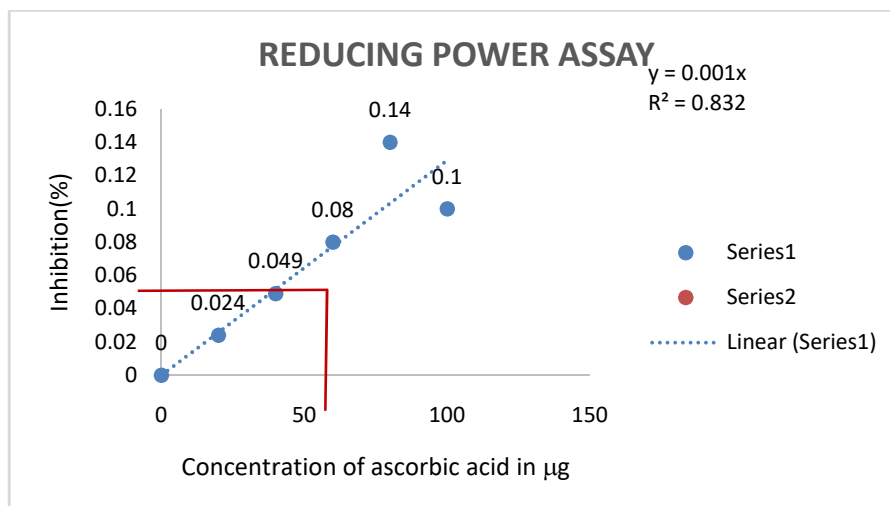


Figure 7: Reducing Power of Methanolic Seed Extract

d) Anti-Inflammatory Activity

i. Lipoxygenase (15-Lox) Inhibition

The methanol extracts of *Carica papaya* exhibited potent capacity inhibiting 50% LOX activity with an IC_{50} value of 47 μ g.

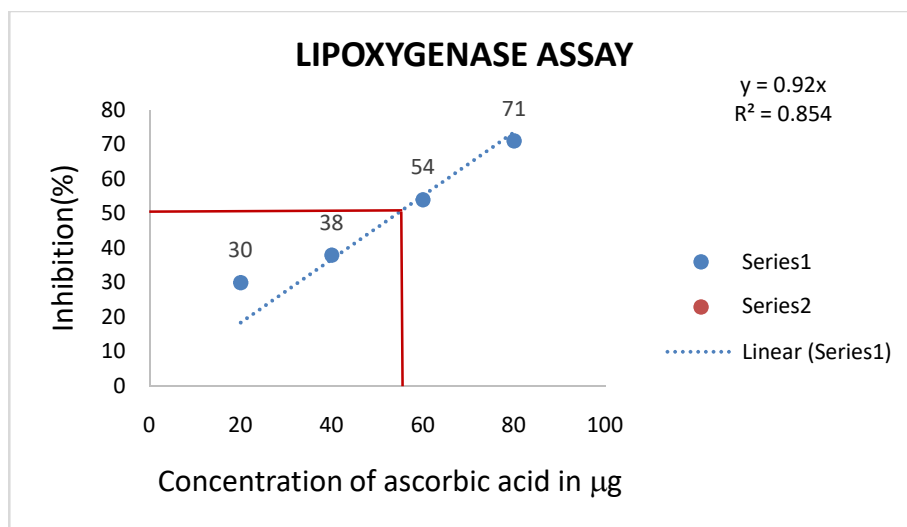
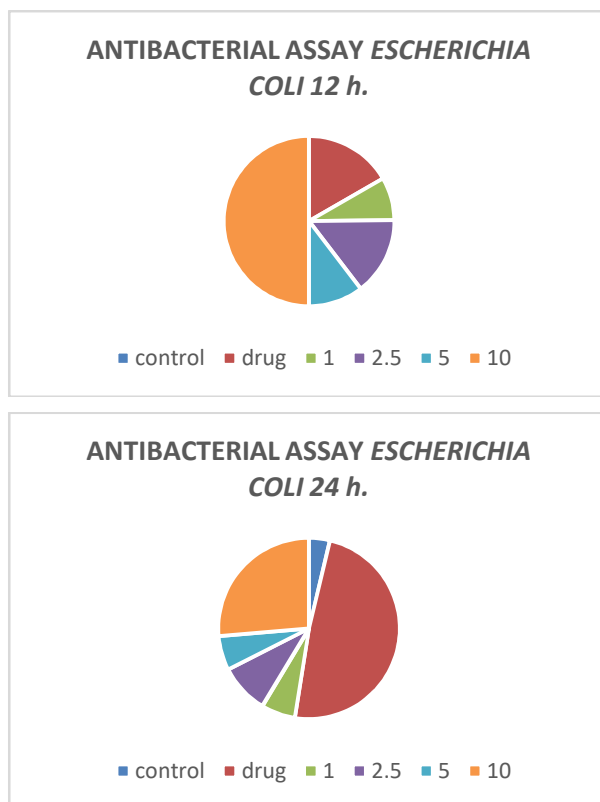


Figure 8: 15- LOX inhibition by methanolic extract of papayaseeds with IC_{50} of 47 μ g

e) Antibacterial Screening

The results of the antibacterial sensitivity of the methanolic extract of *C. papaya* seed by disc diffusion method are depicted for different time intervals of 12, 24 and 48 h in the graph for *Escherichia coli* (Fig. 9) and *Pseudomonas Vulgaris* (Fig. 10). The results reveal that the extract has antimicrobial activity against these pathogenic organisms studied. The antibacterial

activity was screened from the zone of inhibition. The four different concentrations of methanolic extract (1, 2.5, 5 and 10 mg) inhibited *Escherichia coli* (Table 3; Fig. 11) *Pseudomonas Vulgaris* (Table 4; Fig. 12) growth with a maximum inhibition at 10mg. The streptomycin drug used showed maximum growth inhibition (3.94mm) compared to control (methanol, 10 ml). The drug inhibited *Escherichia coli* (2.95mm).



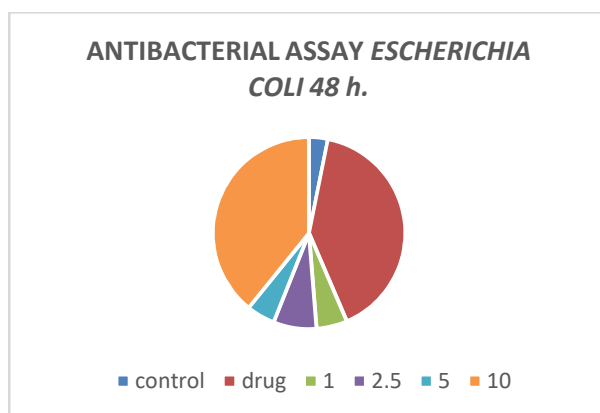


Figure 9: Results of methanolic seed extract inhibiting *E. coli* at different time intervals

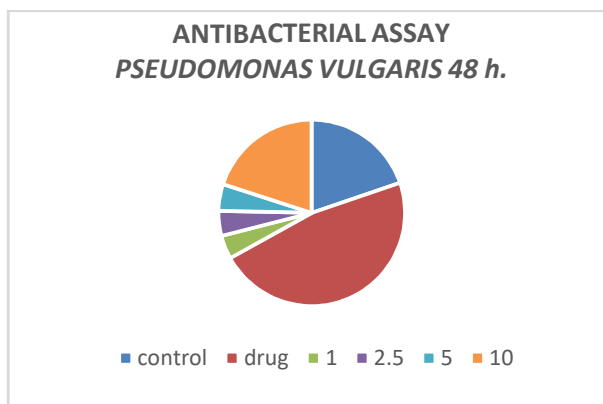
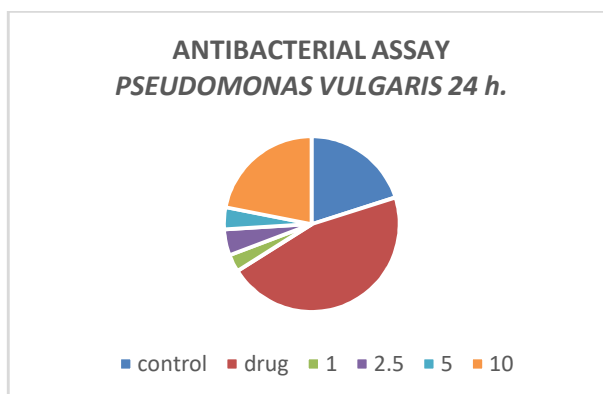
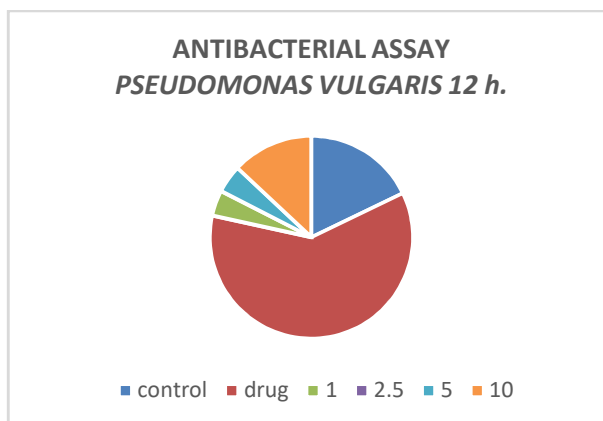


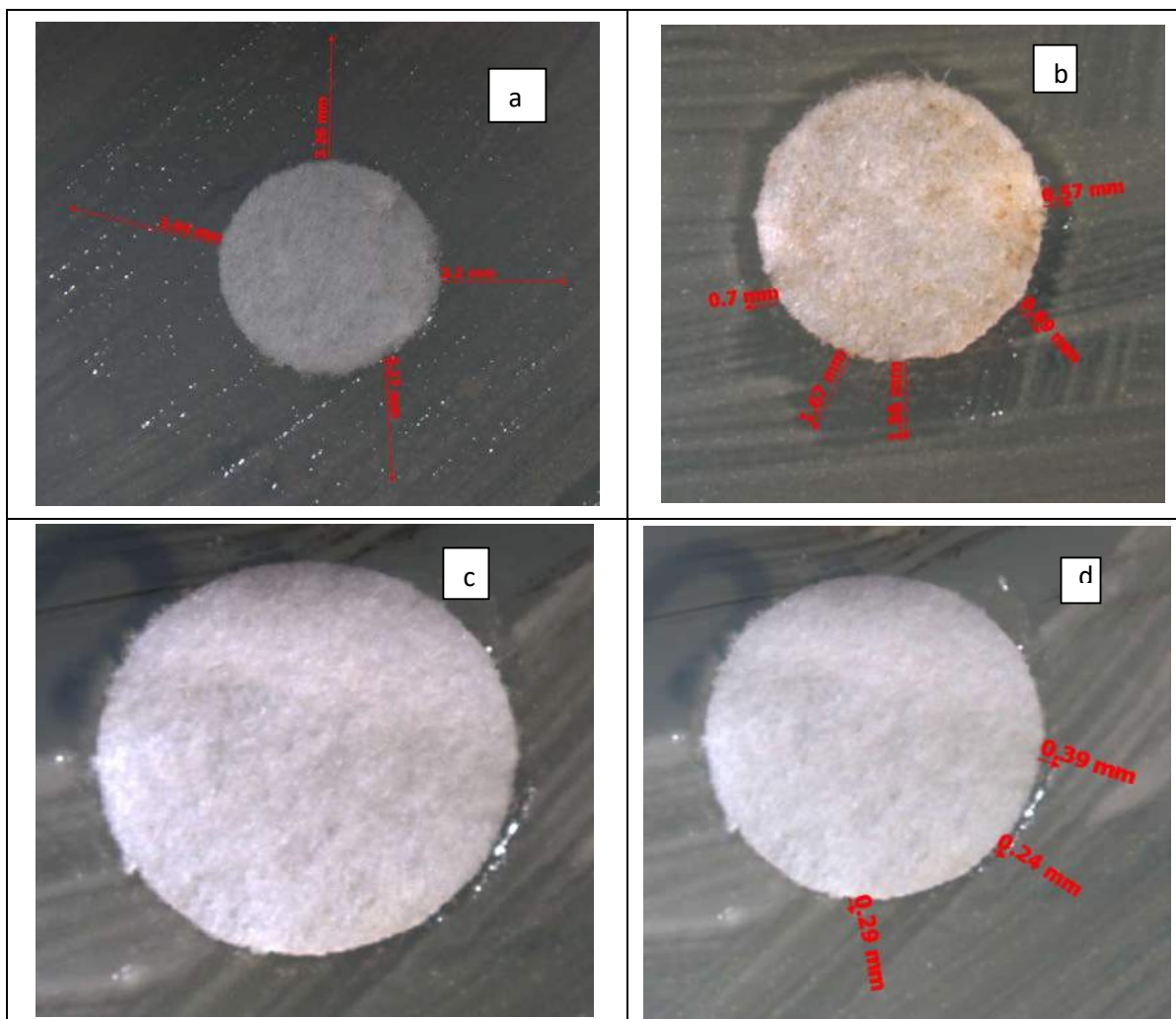
Figure 10: Results of methanolic seed extract inhibiting *Pseudomonas vulgaris* at different time intervals

Table 2: Antimicrobial activity of papaya seed methanolic extract for *Escherichiacoli*

SI No.	Solvent Used	Concentration	Zone of Inhibition			
			T(0h)	T(12h)	T(24h)	T(48h)
1	Methanol	CONTROL	0.0	0.0mm	0.20mm	0.23mm
	Spteromycin	DRUG	0.0	0.45mm	2.63mm	2.95mm
		1 μ l	0.0	0.22mm	0.33mm	0.38mm
		2.5 μ l	0.0	0.4mm	0.48mm	0.53mm
		5 μ l	0.0	0.28mm	0.33mm	0.35mm
		10 μ l	0.0	1.35mm	1.42mm	2.86mm

Table 3: Antimicrobial activity of papaya seedmethanolic extract for *Pseudomonas vulgaris*

SI No.	Solvent Used	Concent Ration	Zone of Inhibition			
			T(0h)	T(12h)	T(24h)	T(48h)
1	Methanol	Control	0.0	0.96mm	1.43mm	1.65mm
	Streptomycin	Drug	0.0	3.26mm	3.27mm	3.94mm
		1 μ L	0.0	0.22mm	0.23mm	0.34mm
		2.5 μ l	0.0	0.0mm	0.34mm	0.36mm
		5 μ l	0.0	0.24mm	0.29mm	0.39mm
		10 μ l	0.0	0.7mm	1.56mm	1.67mm



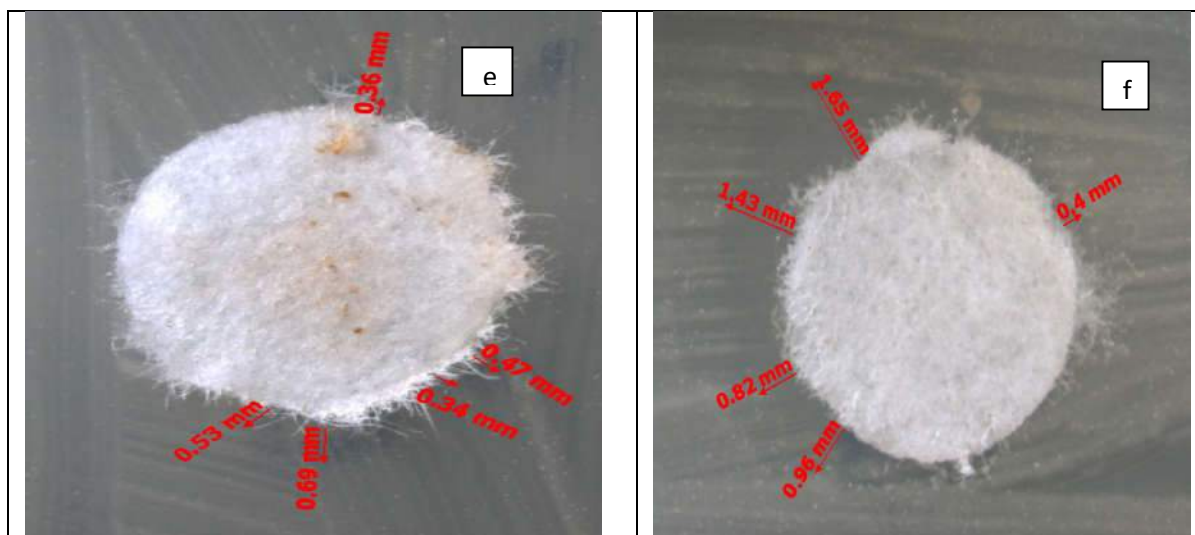
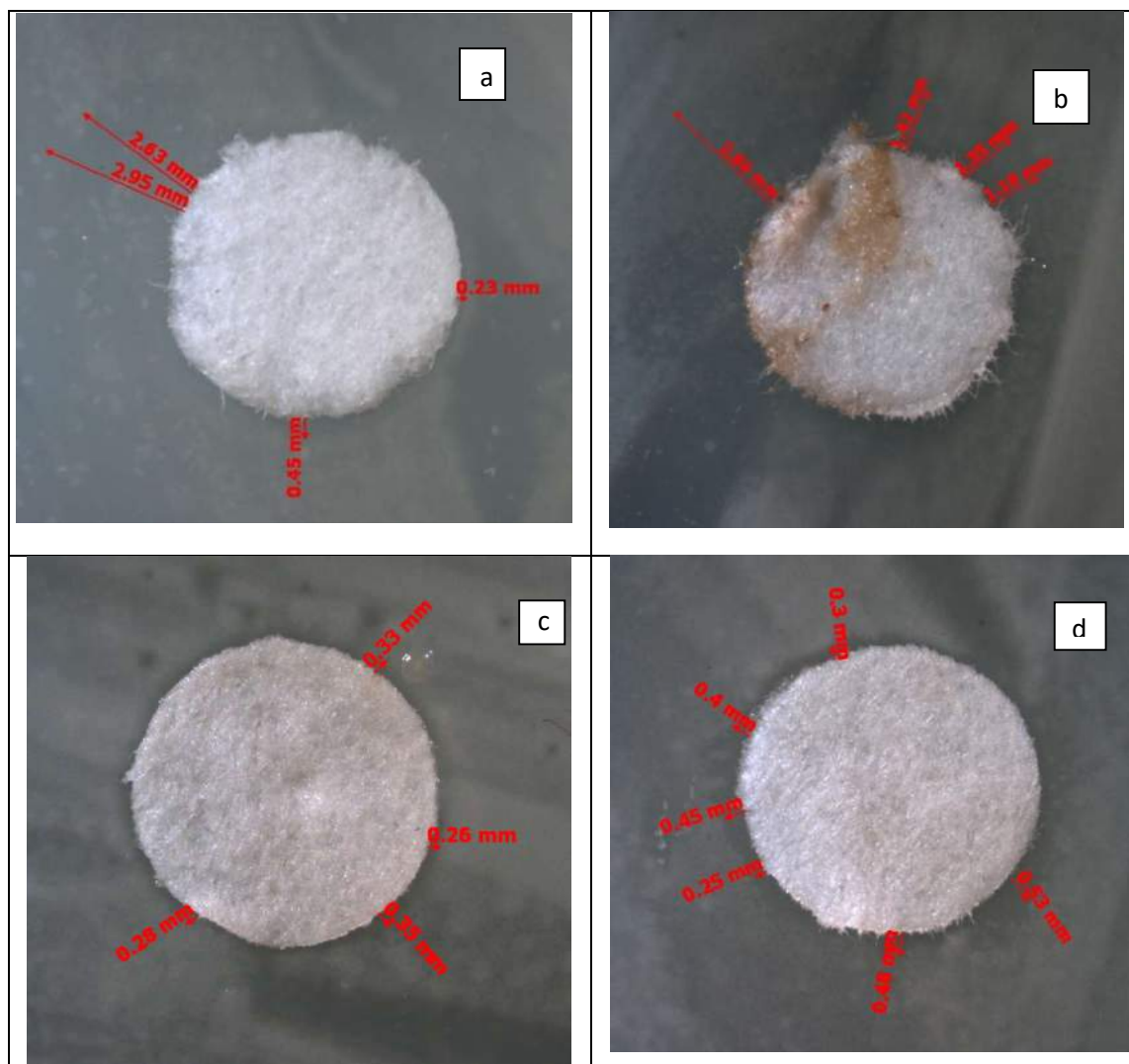


Figure 11: Inhibition capacity of methanolic extracts for *Escherichiacoli* at concentration of 1 ug (c); 2.5 ug (d); 5 ug (e); and 10 ug (f) in comparison to control used methanol (a) and drug, streptomycin (b)



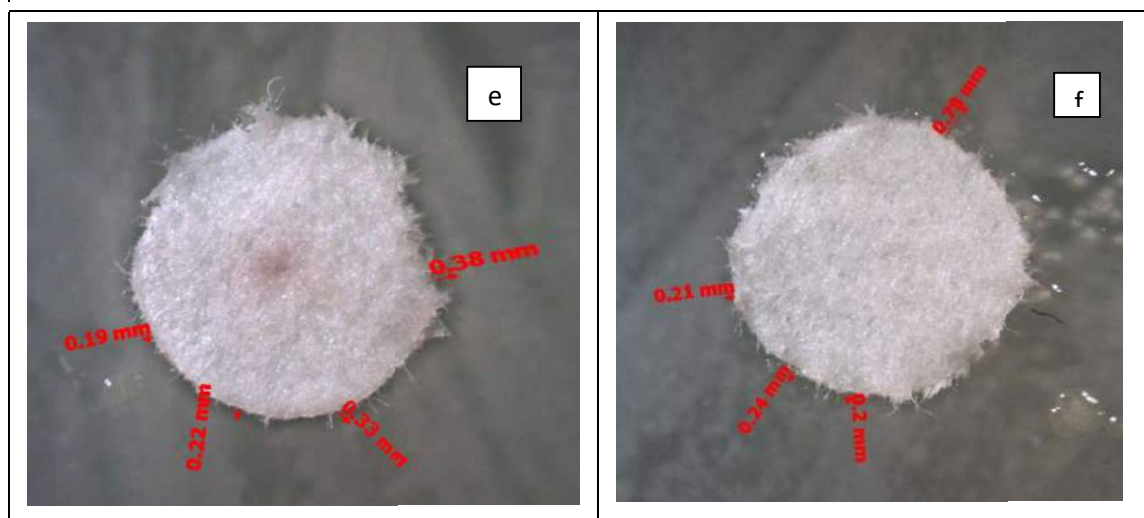
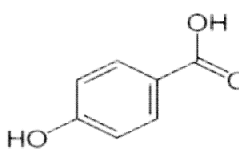
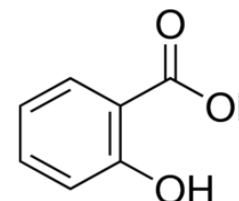
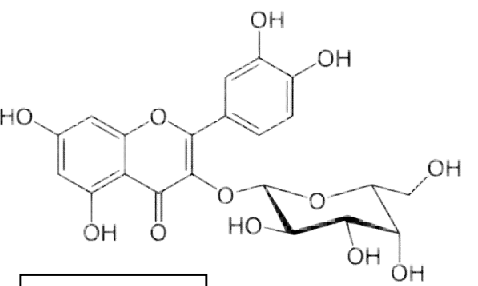
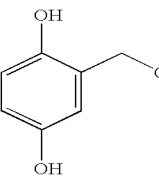
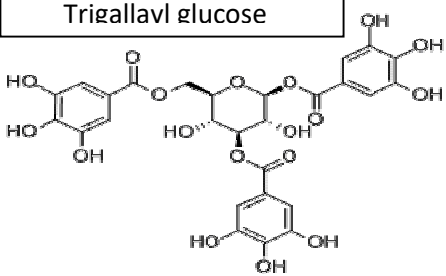
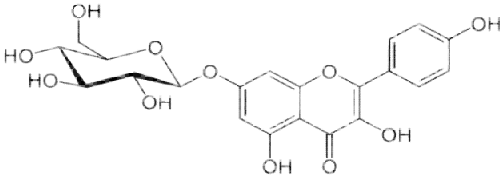


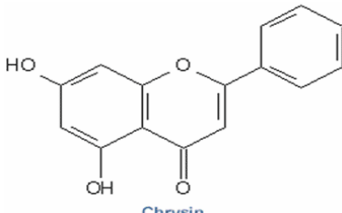
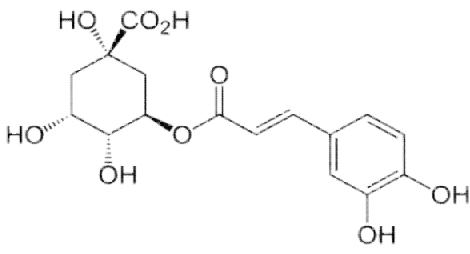
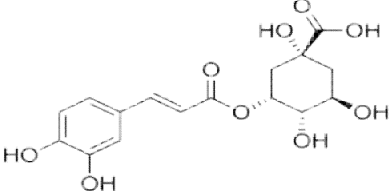
Figure 12: Inhibition capacity of methanolic extracts at concentration of 1 ug (c); 2.5 ug (d); 5 ug (e); and 10 ug (f) in comparison to control used (methanol; a) and drug, streptomycin (b)

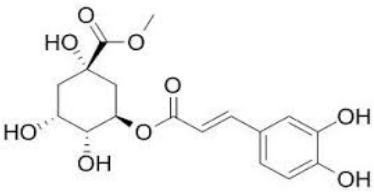
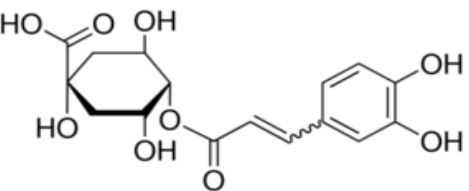
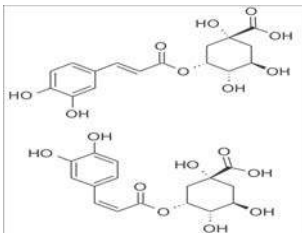
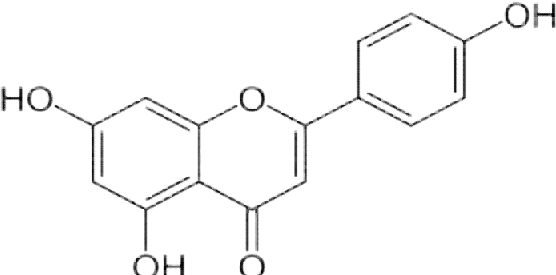
- f) Profiling of Compounds in methanol extract of *Carica papaya* seeds determined by UPLC-PDA-ESI/HDMS
Identification of metabolites based on chromatographic and in-house MS data identified 6 metabolites *p*-hydroxybenzoic acid, salicylic acid, hyperoside, gentisyl alcohol, trigalloyl glucose, kaemferolhexoside (Table 5) by comparison of retention time and MS/MS data.

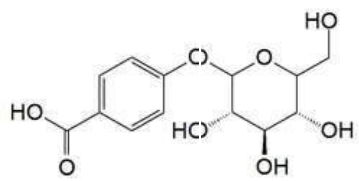
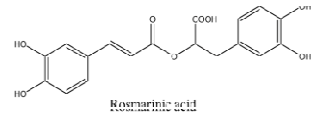
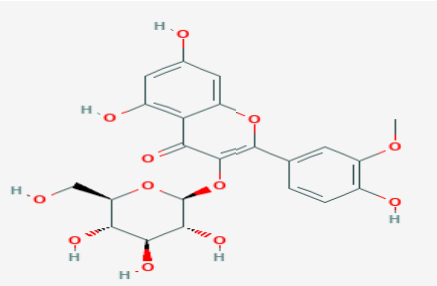
Table 4: Putative compounds identified by UPLC-PDA-ESI/HDMS

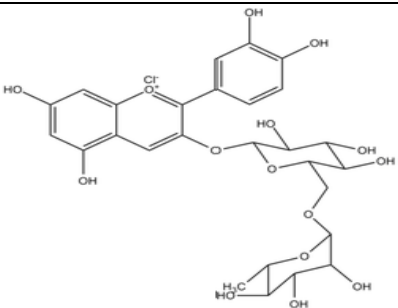
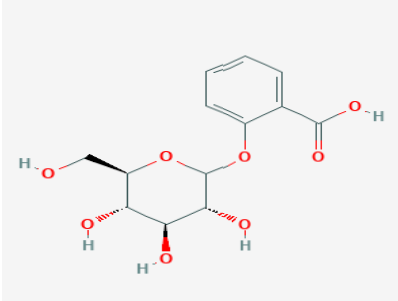
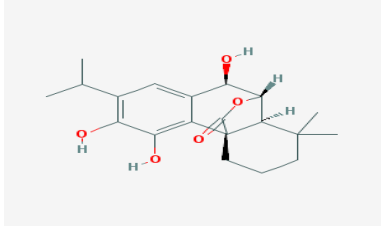
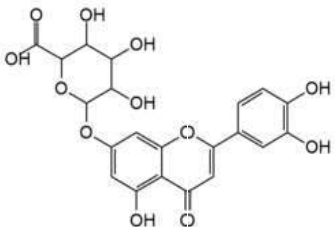
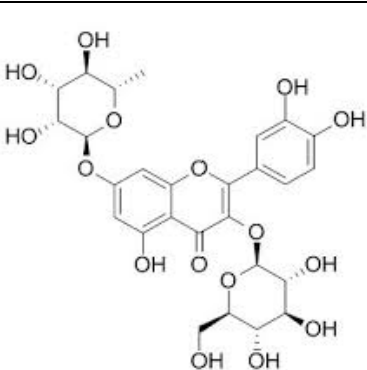
M/Z Ratio	Molecules	Structures
137 138 462-463 407-408	<i>p</i> -hydroxy benzoic acid Salicylic acid Hyperoside Gentisyl alcohol Glucosyl and benzoyl groups intact	 <p>p-hydroxy benzoic acid</p>  <p>Salicylic acid</p>  <p>Hyperoside</p>
		 <p>gentisyl alcohol</p>

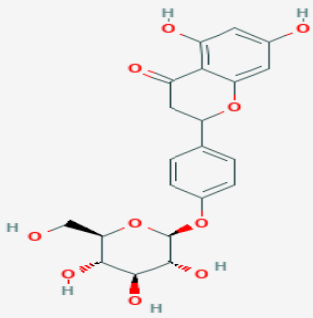
279,280,635, 115,116,117, 253,293,353, 359,277,278, 279,377,554, 642,297,265, 269,299,298, 357,358,393, 476,531,595, 688,281,311	Trigalloyl glucose Luteolin 8-C(2-malonyl glucoside) Kaempferol hexoside	<div>Trigallavl glucose</div>   <div>Kaempferol hexoside</div>
353,406,547, 605,639,440, 995,831,738, 116,355,311, 368,402,833		

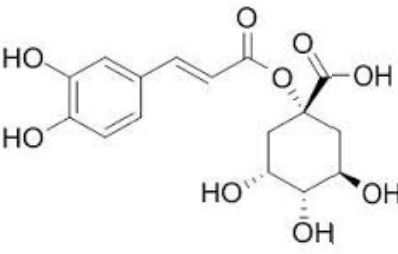
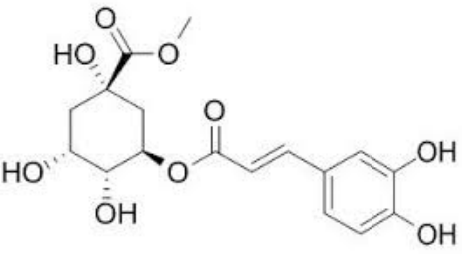
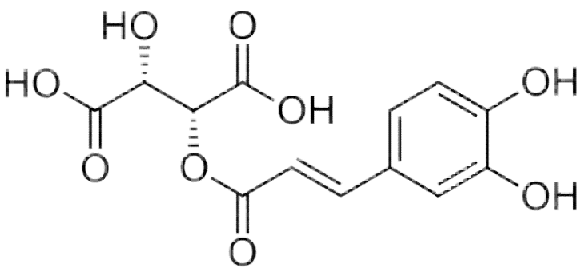
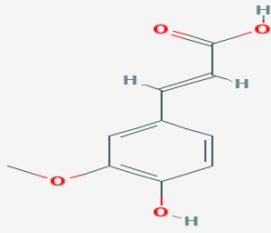
m/z	Molecules	Structures
253	Chrysin	 Chrysin
353	Chlorogenic acid	
355	Neochlorogenic acid	

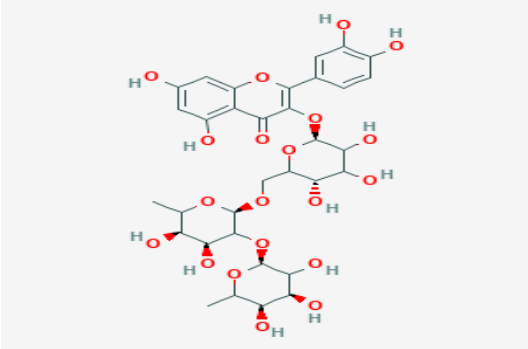
	3-O-Caffeoylquinic acid	
	4-O- Caffeoylquinic acid	
	5-O- Caffeoylquinic acid	
269	Apigenin	

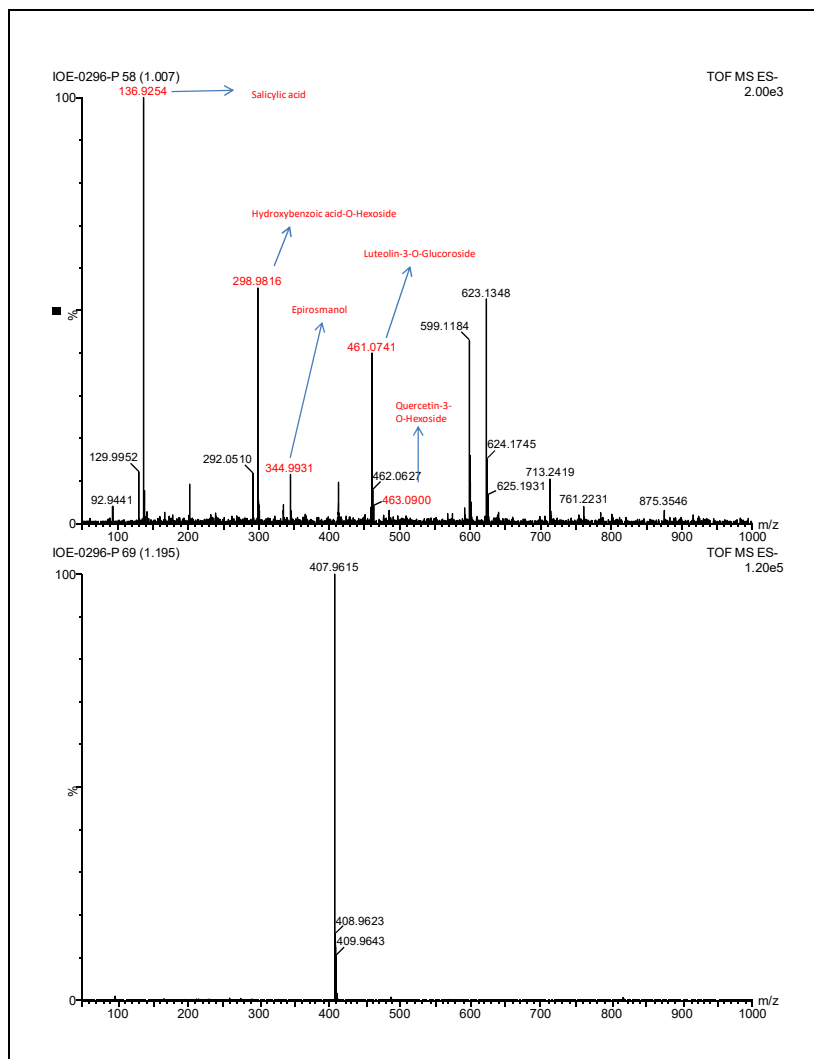
299	Hydroxybenzoic acid –O- hexoside	
358	Rosmarinic acid	
477	Isorhamnetin-3-O- hexoside	

595	Cyanidin-3-O- rutinoside	
136	Salicylic acid	
345	Epirosmanol	
461	Luteolin-3-O-glucuronide	
463	Quercetin-3-O- hexoside	

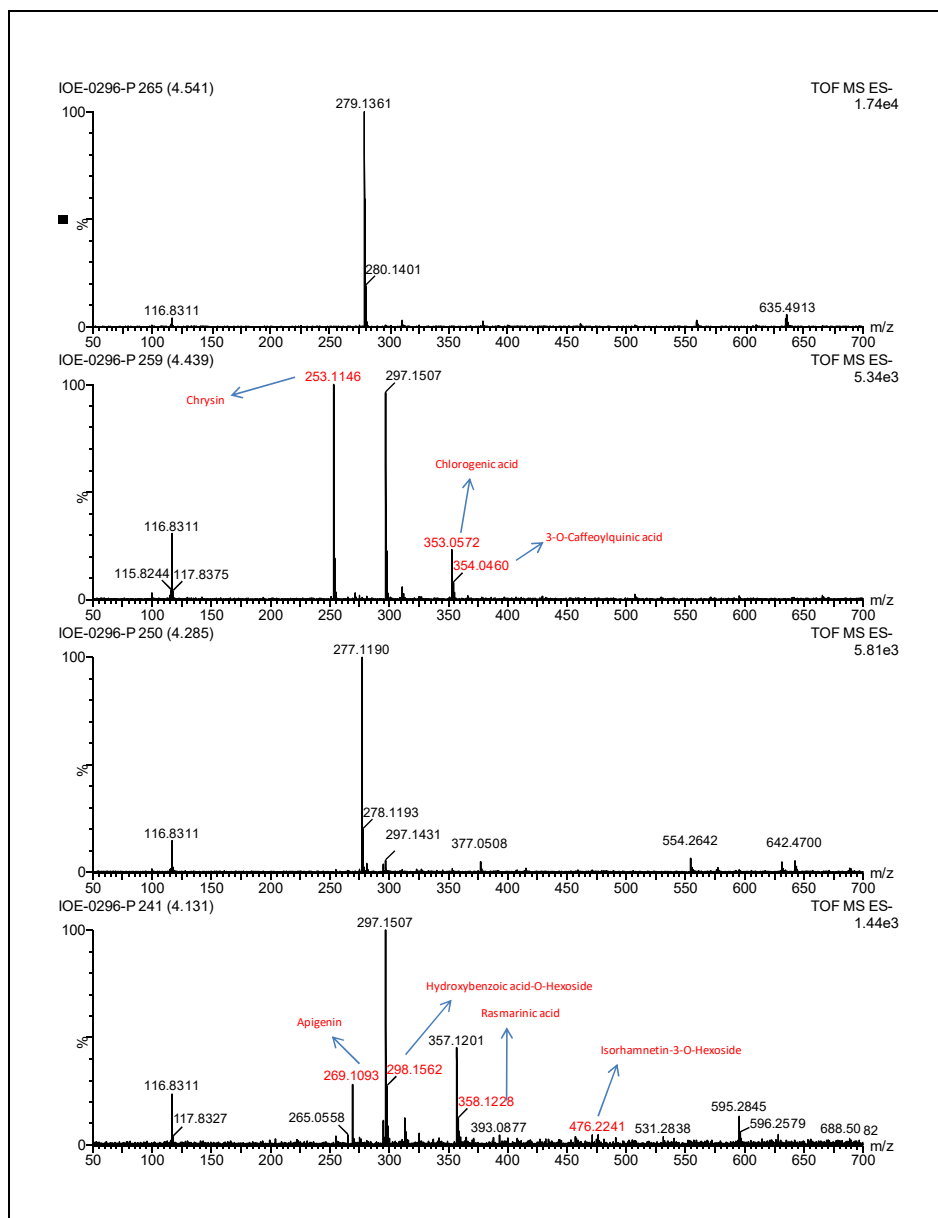
270	Naringenin	
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354	1-Caffeoylquinic acid	
	3-Caffeoylquinic acid	
311	Caftaric acid	
355	Ferulic acid-0- hexoside	

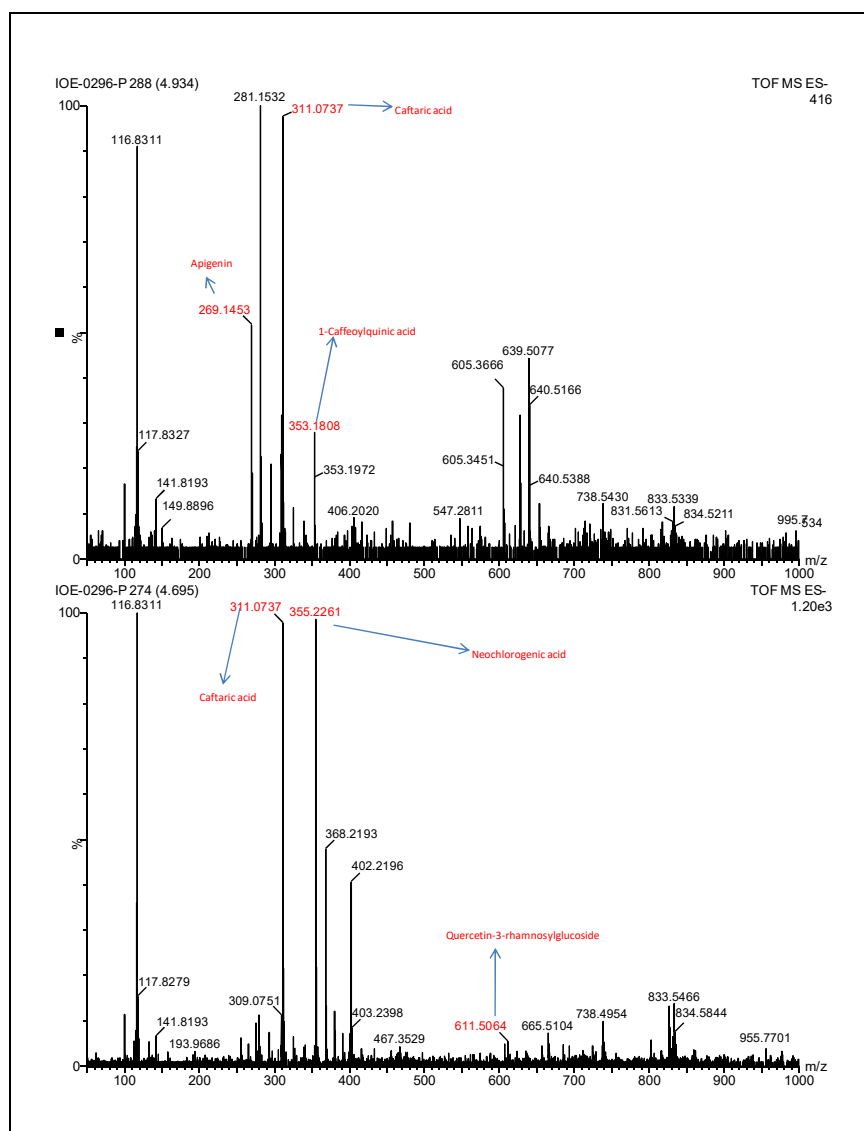
611	Quercetin-3-rhamnosylglucoside	
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P-MS1



P-MS2



P-MS3

YP T

The constituent of the extract of *C. papaya* (dried) seeds contain compounds and micronutrients which may be responsible for its observed antioxidant activity. This study suggests that the plant possesses antioxidant activities that can counteract the oxidative damage. The total phenol test provides information on the reactivity of the seed extract with a stable free radical. It gives a strong absorption band. The degree of reduction in absorbance measurement is indicative of the radical scavenging (antioxidant) power of the extract. The extract of *Carica papaya* appeared to be as potent as Gallic Acid with maximum inhibition. The extract is found to have broad-spectrum antibacterial activity and used as analgesics and narcotics for pain relief. A report indicates that extracts are more active against Gram-positive bacteria than Gram-negative bacteria while that of the leaf extract

of *C. papaya* was next to the most sensitivity with Gram-negative bacteria[17]. The activity of the extract is comparable to those of antibiotics. The demonstration of activity against the test bacteria provides scientific bases for the local usage of the plant in the treatment of various ailments. The fact that the extract is active against Gram-positive bacteria and Fungi tested may indicate a broad spectrum of activity. This observation is very significant because of the possibility of developing therapeutic substances that will be active against multidrug-resistant organisms.

Lipoxygenases (LOXs) are a family of non-heme iron-containing dioxygenases catalyzing the biosynthesis of leukotrienes. Leukotrienes function as initiators of inflammation and their inhibition is partly responsible for the anti-inflammatory activity. In the present study methanolic extracts, *Carica papaya* showed good anti-LOX activity with an IC₅₀ value of

47 μ g.LOX inhibition was used to evaluate the anti-inflammatory activity of a few medicinal plants[10].

Plant phytochemicals with health benefits have been attributed to health as they cannot be synthesized by humans and they have been linked to antioxidant activity. In the present study, UPLC-DAD identified *p*-hydroxybenzoic acid, salicylic acid, hyperoside, gentisyl alcohol, trigalloyl glucose, kaemferolhexoside among others. These are reported as the strongest natural anti-inflammatory agent[13]. The presence of the phytochemicals in the extract could also support the therapeutic property tamarind seed for the mentioned application in the traditional literature of India.

YP S

Carica papaya is a nutraceutical plant having a wide range of pharmacological activities. The whole plant has its own medicinal value. The wide range of enzymes, vitamins present in *Carica papaya* makes it a nutraceutical plant. Antioxidant and antimicrobial properties of methanolic extract of *Carica papaya* have recently been of great interest in both the research and food industry, because of its possible use as natural additives which emerged from a growing tendency to replace synthetic antioxidants with natural ones. Owing to the antioxidant and antibacterial activities exhibited by the seed extract investigated in this study, it could be considered a natural herbal source that can be used in the food and pharmaceutical industries. However, further studies are needed to obtain purified compounds that may be responsible for the activities observed from the tested seeds.

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Exclusive

Reputation



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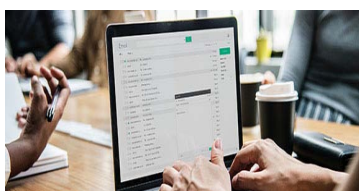
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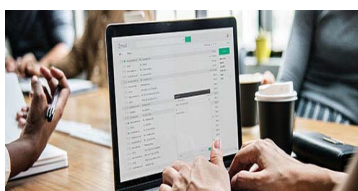
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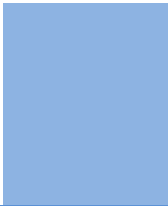
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3. Ensure corresponding author's email address and postal address are accurate and reachable.
4. Manuscript to be submitted must include keywords, an abstract, a paper title, co-author(s) names and details (email address, name, phone number, and institution), figures and illustrations in vector format including appropriate captions, tables, including titles and footnotes, a conclusion, results, acknowledgments and references.
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- Any other original work

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2. Drafting the paper and revising it critically regarding important academic content.
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Acknowledgments

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Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.



Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

- a) A title which should be relevant to the theme of the paper.
- b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
- c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
- d) An introduction, giving fundamental background objectives.
- e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
- f) Results which should be presented concisely by well-designed tables and figures.
- g) Suitable statistical data should also be given.
- h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

- i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
- j) There should be brief acknowledgments.
- k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.



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It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

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The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, "What words would a source have to include to be truly valuable in a research paper?" Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.



Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

PREPARATION OF ELETRONIC FIGURES FOR PUBLICATION

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

TIPS FOR WRITING A GOOD QUALITY COMPUTER SCIENCE RESEARCH PAPER

Techniques for writing a good quality computer science research paper:

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of computer science then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

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6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.



20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium through which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

INFORMAL GUIDELINES OF RESEARCH PAPER WRITING

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.



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- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.



The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

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Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.



Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

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- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

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Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."



Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

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Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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