3.3.1 Number of research papers published per teacher in the Journals notified on UGC CARE list during the last five years

3.3.1.C CalendarYear-2020

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MGV's PHARMACY COLLEGE PANCHAVATI NASIK-3

PRINCIPAL
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1.Name of Faculty: Dr.R.S.Bhambar

Original Article

Effect of Vanillic Acid on Nerve Conduction Velocity in Chronic Constriction Injury Model of Neuropathy

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ABSTRACT

Background: Neuropathic Pain (NP) is less or symptomatically managed by presently available therapeutics. Therefore developing more effective drugs with minimum adverse effects is essential. Vanillic acid is phenolic secondary plant metabolite. Extensive research regarding phenolic acids with antioxidant, free radical scavenging and neuroprotective roles have been published. **Objectives:** The aim of this undertaken study was to evaluate the efficacy of vanillic acid (V.A.) to improve nerve conduction velocity in neuropathic pain induced by CCI (chronic constriction injury) and to evaluate its antioxidant potential. **Methods:** Rats were divided into 7 groups ($n = 6$), as negative control, positive control (CCI), sham control, CCI + gabapentin (300 mg/kg, p.o.), V.A. (25 mg/kg, p.o.), V.A. (50 mg/kg, p.o.) and V.A. (100 mg/kg, p.o.). After surgery oxytetracycline (25 mg/kg, i.m.) was administered in animals to avoid any infection. Vanillic acid and gabapentin administered post-surgery from day 4th till 28th day. Velocity of nerve conduction and antioxidant and histopathological studies were conducted on 28th day. **Results:** Repeated oral administration of vanillic acid (50 mg/kg, 100 mg/kg) significantly improved MNCV. V.A. showed antioxidant property by significantly elevating level of GSH and also reversed histopathological changes induced by CCI. **Conclusion:** This study has suggested antioxidant and neuroprotective effect of vanillic acid in CCI induced peripheral neuropathy.

Key words: CCI, MNCV, Neuropathy, Gabapentin, Vanillic acid.

INTRODUCTION

Neuropathic Pain (NP) is initiated or caused by neuronal injury or functional disabilities in the nervous system.[1] NP is arising from damage to nerve due to tumors, diabetic neuropathy, herpes zoster, complex regional pain syndrome, AIDS, hypoxia.etc.[2] NP majorly affects quality of life of patients and has a great economic and social impact. It is reported by the institute of medicines that millions of American adults usually suffer from chronic pain and 17.9% suffer from neuropathic pain.[1] NP is multifactorial causing impairment in nerve function. The pathophysiology of pain is complex and involves central and peripheral pathways viz. neurotransmitter release, alteration in expression of ion channels and pain pathway.[4] It is known that both hyperalgesia and allodynia coexist in both, inflammatory and neuropathic pain.[5] Physiological stress caused by metabolic disorders, various inflammatory responses, viral infections, direct neuronal trauma, diseases like cancer or use of chemotherapeutic drugs and primary neurological diseases leads to neuronal functional disabilities and damage resulting into NP. Pain may be triggered by even any non-specific, small intensity stimulus, as neuronal injury changes neurophysiology to the long extent. These neuronal changes leads to over-expressions of ion channels and/or neuronal receptors generating abnormal action potentials and such synaptic transmission can result in

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Convalescent plasma: A possible treatment protocol for COVID- 19 patients suffering from diabetes or underlying liver diseases

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ABSTRACT

Background & Aim: As on date, no specific treatment is available for devastating COVID-19 (SARS-CoV-2) infection. This pandemic viral infection has affected over 200 countries within a very short time and created a calamitous situation across the globe. As per WHO guidelines, the treatment is mainly symptomatic and supportive. This clinical protocol has not proven sufficient to save the lives of COVID-19 patients suffering from diabetes or having underlying liver diseases; hence there is utmost need to tackle this situation by other means such as Convalescent Plasma (CP) therapy.
Methods: A comprehensive literature survey was carriedout using Elsevier, PubMed, Taylor & Francis, Springer, Nature and Google search engines.
Results: The patients suffering from diabetes or liver dysfunction or any other underlying diseases are at greatest risk of SARS-CoV-2 infection. From the study, it is proved that plasma collected from the recovered patients of viral infection has considerable potential to treat the viral disease without the occurrence of adverse effects.
Conclusion: The CP therapy can be a possible life saving alternative to treat critical COVID-19 patients having diabetes or underlying liver dysfunction. Hence, randomised clinical trials are recommended at the earliest to save the lives of infected individuals of COVID- 19.

1. Introduction

A novel Coronavirus disease 2019 (COVID-19) is the infection of the respiratory tract caused by Severe acute respiratory syndrome coronavirus – 2 (SARS-CoV-2) which has created a disastrous situation in most of the countries. The first case of COVID-19 was reported in China's Wuhan State (capital of Hubei province) in December 2019 [1].

It is a highly infectious disease and almost reached every country across the globe (Over 200 counties) within a very short span. By April 20, 2020 over 24 lakh people were infected with COVID-19 and caused over 1.7 lakh deaths worldwide [2]. The mortality rate based on the cases which had an outcome is on higher side, i.e. 20% [2]. Most of COVID-19 patients were asymptomatic (or with very mild symptoms) and recovered themselves, which were very difficult to be detected; otherwise the total number of COVID-19 cases reported so far would be on the higher side. As on date, no effective therapy is available to treat devastating SARS-CoV-2, the treatment is mainly experimental or empirical.

According to the figures of the International Diabetes Federation, more than 463 million peoples were suffering from diabetes globally [3]. Very limited data is available regarding COVID-19 patients with diabetes, but it is reported that the diabetic patients are at the utmost risk of SARS-CoV-2 infection. The recent report published by Chinese Centre for Disease Control and Prevention of

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M.G.V.'S PHARMACY COLLEGE PANCHAVATI NASIK-3

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Protective effect of SKB_Gutbiotic against castor oil and *E.coli* induced diarrhea in laboratory animals

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ABSTRACT

The aim of this study is to evaluate antidiarrheal activity of SKB_Gutbiotic against Castor oil and *E.coli* induced diarrhea in Swiss albino mice and Sprague Dawley rats. In present study three doses of SKB_Gutbiotic were tested against castor oil induced diarrhea in mice. Its effect on co-administration with L-arginine was studied. SKB_Gutbiotic delayed onset of diarrhea, reduced fecal output and fecal weight. In Gastrointestinal transit time and Castor oil induced enteropooling, SKB_Gutbiotic significantly reduced peristaltic index and volume of intestinal content respectively. In *E.coli* induced diarrhea model, *E.coli* suspension was administered for 3 days for inducing diarrhea. SKB_Gutbiotic significantly and dose dependently reduced fecal output, improved fecal consistency, reduced fecal water content and improved WBC count. Histopathological images showed improvement in damage caused to the mucosal epithelium due to *E.coli* and also improved complete crypt cell architecture and integrity of goblet cells. These results indicated that SKB_Gutbiotic can be used as an antidiarrheal agent against castor oil and *E.coli* induced diarrhea. It inhibits colonization of *E.coli* bacteria on colonic epithelium which results into decreased intestinal hypersecretion and motility which is very useful in the management of infectious diarrhea. Thus SKB_Gutbiotic could be an effective alternative to standard antidiarrheal drugs.

1. Introduction

Diarrhea a word derived from greek (dia-through) and latin (rheein-to flow or run). It is characterized by increase in intestinal motility with discharge of semisolid or watery feces 4 to 5 times a day in animals. It involves increase in intestinal fluid volume, frequency of bowel movement, wet stool and abdominal cramps, leading to loss of electrolytes and water [1]. Infectious agents including bacteria, viruses and parasites causes diarrhea. *E.coli*, rotaviruses are major agents causing diarrhea in farm animals. This enteropathogen causes specific enteric infection that is associated with non-specific signs of diarrhea. Infectious diarrhea in farm animals is one of the most common and economically devastating conditions, encountered in animal agriculture industry [2]. It is both preventable and treatable. A significant proportion of diarrheal diseases can be prevented through safe drinking water and adequate sanitation and hygiene. Diarrhea is usually a symptom of an infection in intestinal tract, which can be caused by a variety of bacterial, viral and parasitic organisms which leads to disruption in intestinal, absorptive and secretary functions. Bacterial infections are likely to account for an increasing proportion of all diarrhea-associated deaths [3]. Diarrhea is classified etiologically into two categories-infectious and non-infectious diarrhea [4]. Non-infectious diarrhea can be caused by toxins, chronic diseases, or antibiotics. Infectious diarrhea occurs worldwide in humans as well as animals due to variety of bacteria. Rotavirus and *E. coli* strains are non-toxin producing bacteria associated with acute and protracted diarrhea in infants particularly in developing countries. *E.coli* is a major etiological agent involved in infectious diarrhea in humans and animals from different pathogenic characters of *E.coli* divided in 4–5 categories, Enteropathogenic *E.coli* (EPEC), Enterohemorrhegic *E.coli* (EHEC), Enteroaggregative *E.coli* (EAEC), Enteroinvasive *E.coli* (EIEC), Enterotoxigenic *E.coli* (ETEC) [5,6]. EPEC is the leading cause of infectious diarrhea in human as well as farm animals. It is the colonizing intestine which leads to disruption in intestinal pathogenic barrier [7]. EPEC strains are non-toxin producing bacteria associated with acute and protracted diarrhea in infants, particularly in the developing countries. Both EHEC and EPEC bind to the surface epithelia, induce rearrangements of the cytoskeleton referred to as attaching and effacing lesions,

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Effect of *Solanum torvum* Swartz on diabetic neuropathy in alloxan-induced diabetic rats

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Solanum torvum Swartz is a well-known traditional herbal medicinal plant used in diabetes and diabetes-related complications. The objective of the study was to evaluate the effect of *S. torvum* on diabetic neuropathy in alloxan-induced diabetic rats. Diabetes was induced in Wistar rats by using a single intraperitoneal injection of alloxan monohydrate (150 mg/kg, i.p.). After confirmation of diabetes, rats received metformin (120 mg/kg, p.o.) and STME (30 and 100 mg/kg, p.o) for 5 weeks. Diabetic rats showed significant (P <0.05) behavioural changes, increase in blood glucose levels, decrease in relative organ weight of pancreas, significant (P <0.05) decrease in reduced glutathione (RGSH) and significant (P <0.05) increase in TBARS levels. While STME (100 mg/kg) treated diabetic rats significantly (P <0.05) reversed the above parameters as compared to diabetic rats. Treatment with STME (100 mg/kg) has also reversed histopathological changes as observed in diabetic control rats. The study suggests that methanolic extract of *S. torvum* ameliorates diabetic neuropathy in alloxan-induced diabetic rats.

Keywords: Alloxan monohydrate, Diabetic neuropathy, Metformin, *Solanum torvum*.

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Introduction

Diabetic neuropathy (DN) is a chronic complication of both type I and type II diabetes mellitus (DM). Patients with long term diabetes may develop complications affecting the eyes, kidneys or nerves (microvascular complications) or major arteries. Diabetic neuropathy is nerve damaging disorder associated with DM. Neuropathic pain is characterized by the sensory abnormalities such as unpleasant abnormal sensation (dysesthesia), an increased response to painful stimuli (hyperalgesia), and pain in response to the stimulus that does not normally provoke pain (allodynia). Various proposed mechanisms which lead to pathogenesis of DN are activated polyol pathway, AGE's (Advanced glycation end products) formation PKC (Protein kinase C) activation and hexosamine pathway. Hyperglycemia is the primary cause of DN. There has been a major advance in the control of hyperglycemia (diabetes), through dietary changes, hypoglycemic agents, insulin and islet transplantation, even though the long term complication of diabetes, such as neuropathy remains a serious problem[1]. Therefore, agents or compounds that exert multiple actions, such as antioxidants, antidiabetic/hypoglycemic and antiglycation properties could be more effective than agents with a single action[2]. Alloxan-induced diabetes is one of the commonly used models to induce DM in the experimental animal. Alloxan has found to be selectively toxic to pancreatic beta cell as it preferentially accumulates in the beta cells as glucose analogues. In addition, the cytotoxic action of alloxan is mediated mainly by the generation of reactive oxygen species (ROS). Alloxan and its reductive product, dialuric acid, has been noted to develop redox cycle with the formation of superoxide radicals, which undergo dismutation to hydrogen peroxide [3]. Alloxan is the most leading chemical compound used in diabetogenic research. In research, it is used for induction of Type 1 diabetes. Alloxan is urea derivative which causes selective necrosis of β-cells of pancreatic islet. Chemical induction with alloxan appears to be the easiest, reliable and the most practicable method of inducing diabetes mellitus in rodents[4]. It is generally used to induce experimental diabetes in an animal such as rabbits, rats, mice and dogs with different grades of disease severity by varying the dose of alloxan used[5].

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M.G.V'S PHARMACY COLLEGE PANCHAVATI NASIK-3

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Convalescent plasma: A possible treatment protocol for COVID- 19 patients suffering from diabetes or underlying liver diseases

Ashish Yashwantrao Pawar [a, *], Apoorva Prashant Hiray [b], Deepak Devidas Sonawane [c], Rajendra Sudhakar Bhambar [a], Deelip Vishram Derle [d], Yogesh Suresh Ahire [e]

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ABSTRACT

Background & Aim: As on date, no specific treatment is available for devastating COVID-19 (SARS-CoV-2) infection. This pandemic viral infection has affected over 200 countries within a very short time and created a calamitous situation across the globe. As per WHO guidelines, the treatment is mainly symptomatic and supportive. This clinical protocol has not proven sufficient to save the lives of COVID-19 patients suffering from diabetes or having underlying liver diseases; hence there is utmost need to tackle this situation by other means such as Convalescent Plasma (CP) therapy.
Methods: A comprehensive literature survey was carried out using Elsevier, PubMed, Taylor & Francis, Springer, Nature and Google search engines.
Results: The patients suffering from diabetes or liver dysfunction or any other underlying diseases are at greatest risk of SARS-CoV-2 infection. From the study, it is proved that plasma collected from the recovered patients of viral infection has considerable potential to treat the viral disease without the occurrence of adverse effects.
Conclusion: The CP therapy can be a possible life saving alternative to treat critical COVID-19 patients having diabetes or underlying liver dysfunction. Hence, randomised clinical trials are recommended at the earliest to save the lives of infected individuals of COVID-19.

1. Introduction

A novel Coronavirus disease 2019 (COVID-19) is the infection of the respiratory tract caused by Severe acute respiratory syndrome coronavirus –2 (SARS-CoV-2) which has created a disastrous situation in most of the countries. The first case of COVID-19 was reported in China's Wuhan State (capital of Hubei province) in December 2019 [1].

It is a highly infectious disease and almost reached every country across the globe (Over 200 countries) within a very short span. By April 20, 2020 over 24 lakh people were infected with COVID-19 and caused over 1.7 lakh deaths worldwide [2]. The mortality rate based on the cases which had an outcome is on higher side, i.e. 20% [2]. Most of COVID-19 patients were asymptomatic (or with very mild symptoms) and recovered themselves, which were very difficult to be detected; otherwise the total number of COVID-19 cases reported so far would be on the higher side. As on date, no effective therapy is available to treat devastating SARS-CoV-2, the treatment is mainly experimental or empirical.

According to the figures of the International Diabetes Federation, more than 463 million peoples were suffering from diabetes globally [3]. Very limited data is available regarding COVID-19 patients with diabetes, but it is reported that the diabetic patients are at the utmost risk of SARS-CoV-2 infection. The recent report published by Chinese Centre for Disease Control and Prevention of

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Hot Topic

Combating devastating COVID-19 by drug repurposing

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ABSTRACT

Despite advances in drug discovery, viral infections remain a major challenge for scientists across the globe. The recent pandemic of COVID-19 (coronavirus disease 2019), caused by a viral infection with SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), has created a disastrous situation all over the world. As no drugs are available to treat this life-threatening disease and the mortality rate due to COVID-19 is high, there is an utmost need to attempt to treat the infection using drug repurposing. Some countries are against the use of these drugs because of adverse effects associated with drug repurposing and lack of statistically significant clinical data, but they have been found to be effective in some countries to treat COVID-19 patients (off-label/investigational). This article emphasises possible drug candidates in the treatment of COVID-19. Most of these drugs were found to be effective in in vitro studies. There is a need to re-assess in vitro data and to carry out randomised clinical trials. Further investigations of these drugs are recommended on a priority basis.

1. Introduction

COVID-19 (coronavirus disease 2019) is a respiratory tract infection caused by a novel coronavirus that was first identified in the city of Wuhan, Hubei Province, China, at the end of 2019. Genetically, the virus closely resembles the severe acute respiratory syndrome coronavirus (SARS-CoV) [1] and has been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has spread across the globe to more than 190 counties within a short period, i.e. within 45–90 days of its initial recognition. The COVID-19 pandemic has created a devastating situation not only in developing countries but also in developed nations. To date, there is no specific treatment available to treat infection with SARS-CoV-2 and the disease COVID-19.

By the end of March 2020, approximately 750 000 people have been infected with SARS-CoV-2 globally and the situation is overwhelming in countries such as China, Italy, Spain and the USA. As no specific treatments or vaccine for COVID-19 are available, there is a need of drug repurposing, where approved drugs can be effectively used to treat novel diseases with minimal or no side effects. The benefits of drug repurposing are that the safety, optimal dosage and pharmacokinetics of drugs are well known.

In India, most of the drugs and antibiotics used to treat COVID-19 have been repurposed (off-label/investigational use) and have been found to be very effective in affected individuals. This might be one of the reasons for the low mortality rate in India (0.02 deaths per million persons) compared with Italy (178 deaths per million persons) [2].

Chloroquine and its hydroxyl analogue hydroxychloroquine have been reported for their use as an antiviral agent in various studies. Apart from their antimalarial use, they have also shown in vitro activity against SARS-CoV-2 [3,4]. The pH increase induced by chloroquine and hydroxychloroquine within acidic organelles such as lysosomes, endosomes and Golgi vesicles is responsible for their antiviral activity [3,4]. In one mechanism of action, these drugs mainly inhibit virus entry into their host cell by a pH-dependent step. In another mechanism of action, chloroquine and hydroxychloroquine inhibit post-translational modification of the virus envelope glycoproteins inside the endoplasmic vesicles and trans-Golgi network [3,4]. The major stages of the coronavirus replication cycle and the probable sites of action of different drugs are shown in Fig. 1.

Few researchers are against the use of antibacterial agents and antibiotics to treat viral infections, but drugs such as teicoplanin can inhibit the growth of viruses in human cells [5]. Staphylococci infections can be treated with teicoplanin and it was also shown to be efficacious in the first stage of the Middle East respiratory syndrome coronavirus (MERS-CoV) viral cycle. Teicoplanin mainly inhibits the low-pH cleavage of the spike (S) protein by cathepsin L in the late endosomes, hence preventing viral RNA release and replication of virus [5,6].

Other glycopeptide antibiotics such as oritavancin, dalbavancin and telavancin also have the potential to inhibit the entry of

Abbreviations: CoV, coronavirus; MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus.

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M.G.V.'S PHARMACY COLLEGE PANCHAVATI NASIK-3

7.Name of Faculty:Mrs.S.H.Pawar

Research Article

Effect of Vanillic Acid in Streptozotocin Induced Diabetic Neuropathy

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ABSTRACT

Diabetic neuropathy is a one of the usual complications of both type 1 and 2 diabetes mellitus. Lesion to or diseases of somatosensory system may lead to neuropathic pain which are severally painful. Apart from other etiological factors, the oxidative stress has vital role in the pathogenesis and continuation of diabetic neuropathy. Vanillic acid is the phenolic compound and aromatic secondary plant metabolite. Phenolic acids are proved to have antioxidant and neuroprotective role. So, this study was undertaken to evaluate the effects of vanillic acid on STZ induced diabetic neuropathy by assessing behavioural, biochemical, electrophysiological and histological changes. Diabetes was induced in Wistar rats by using single injection of STZ (55 mg/kg, i.p.). After confirmation of diabetes (blood glucose level >200mg/dl), animals treated with Gabapentin (300 mg/kg, p.o.) and Vanillic acid (25, 50 and 100 mg/kg, p.o) for next 4 weeks. Vanillic acid (50 and 100 mg/kg) treated rats showed significant ($p<0.05$) behavioral changes, decrease in blood glucose levels, significant ($p<0.05$) increase in reduced glutathione (RGSH) level. Treatment with vanillic acid has also reversed histopathological and electrophysiological changes. In conclusion, the present study suggested anti-hyperglycemic, antioxidant and neuroprotective effect of vanillic acid in diabetic neuropathy.

Key words: Hyperglycemia, Hyperalgesia, Allodynia, Diabetes, Vanillic acid, Antioxidants.

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INTRODUCTION

Neuropathic Pain (NP) are chronic pain caused due to damage to nervous system either by injury or diseases. NP is distinguished by the sensory abnormalities viz., dysesthesia (unpleasant abnormal sensation), hyperalgesia (an elevated response to painful stimuli) and allodynia (pain to stimuli that normally does not provoke pain).[1] NP is complication of both types of diabetes. It occurs at about 8% in new patients and more than 50% in patients with long-standing disease.[2] Oxidative stress raised due to chronic hyperglycemia is responsible for diabetic complications like neuropathy. Apoptosis in neurons and supporting glial cells is also developed by this oxidative stress and could be the mechanism causing nervous system damage in diabetes.[3] Reduction in hyperglycemia mediated mitochondrial ROS by certain agents prevent production of advanced glycation end products, glucose-induced activation of protein kinase C, accumulation of sorbitol and activation of NF-B (nuclear factor B) and thus, prevent development of diabetic complications.[4] As most of pain producing stimuli produces neural injury, human experimentation to evaluate of NP is complex. So, animal experimentation is required to understand various mechanisms involved with NP.[5] STZ (Streptozotocin) induced neuropathy is widely accepted model that mimics the diabetic neuropathy. STZ is an anticancer antibiotic and chemically nitrosoureas analogue. STZ

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Original Article

Effect of Vanillic Acid on Nerve Conduction Velocity in Chronic Constriction Injury Model of Neuropathy

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ABSTRACT

Background: Neuropathic Pain (NP) is less or symptomatically managed by presently available therapeutics. Therefore developing more effective drugs with minimum adverse effects is essential. Vanillic acid is phenolic secondary plant metabolite. Extensive research regarding phenolic acids with antioxidant, free radical scavenging and neuroprotective roles have been published. **Objectives:** The aim of this undertaken study was to evaluate the efficacy of vanillic acid (V.A.) to improve nerve conduction velocity in neuropathic pain induced by CCI (chronic constriction injury) and to evaluate its antioxidant potential. **Methods:** Rats were divided into 7 groups ($n = 6$), as negative control, positive control (CCI), sham control, CCI + gabapentin (300 mg/kg, p.o.), V.A. (25 mg/kg, p.o.), V.A. (50 mg/kg, p.o.) and V.A. (100 mg/kg, p.o.). After surgery oxytetracycline (25 mg/kg, i.m.) was administered in animals to avoid any infection. Vanillic acid and gabapentin administered post-surgery from day 4th till 28th day. Velocity of nerve conduction and antioxidant and histopathological studies were conducted on 28th day. **Results:** Repeated oral administration of vanillic acid (50 mg/kg, 100 mg/kg) significantly improved MNCV. V.A. showed antioxidant property by significantly elevating level of GSH and also reversed histopathological changes induced by CCI. **Conclusion:** This study has suggested antioxidant and neuroprotective effect of vanillic acid in CCI induced peripheral neuropathy.

Key words: CCI, MNCV, Neuropathy, Gabapentin, Vanillic acid.

INTRODUCTION

Neuropathic Pain (NP) is initiated or caused by neuronal injury or functional disabilities in the nervous system.[1] NP is arising from damage to nerve due to tumors, diabetic neuropathy, herpes zoster, complex regional pain syndrome, AIDS, hypoxia.etc.[2] NP majorly affects quality of life of patients and has a great economic and social impact. It is reported by the institute of medicines that millions of American adults usually suffer from chronic pain and 17.9% suffer from neuropathic pain.[3] NP is multifactorial causing impairment in nerve function. The pathophysiology of pain is complex and involves central and peripheral pathways viz. neurotransmitter release, alteration in expression of ion channels and pain pathway.[4] It is known that both hyperalgesia and allodynia coexist in both, inflammatory and neuropathic pain.[5] Physiological stress caused by metabolic disorders, various inflammatory responses, viral infections, direct neuronal trauma, diseases like cancer or use of chemotherapeutic drugs and primary neurological diseases leads to neuronal functional disabilities and damage resulting into NP. Pain may be triggered by even any non-specific, small intensity stimulus, as neuronal injury changes neurophysiology to the long extent. These neuronal changes leads to over-expressions of ion channels and/or neuronal receptors generating abnormal action potentials and such synaptic transmission can result in

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