Research Article

Trianthema decandra Root Extract and Cisplatin Action on Biochemical and Histological Characterization of Oral Cancer in DMBA-induced Preclinical Hamster Model

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ABSTRACT

Aim: Chemoprevention, an emerging promising technique for experimental oncology, focuses on the use of natural creates to inhibit or prevent the progression of malignancy. In this study, the chemopreventive ability of TD (*Trianthema decandra*) root extract was studied in regard to DMBA-induced HBPs. **Materials and Methods:** Painted the left Buccal pouches mixture of 0.5% DMBA in liquid paraffin weekly thrice for 14 weeks, and the result was the development of buccal cancer. In hamsters given in two ways, DMBA alone or DMBA+TD root extract treatment, tumour development measurement, detoxification agents, Lipid Peroxidation (LPO), antioxidant status, renal function markers and histological alterations were evaluated. **Results:** Hamsters provided the treatment demonstrated 100% tumour happenings with a DMBA alone causes an imbalance in the Enzymes to break up carcinogens renal function identifiers and cellular redox state. When administered orally to hamsters undergoing DMBA medication, TD root extract, entirely prevented the formation of tumors and Cellular redox state and enzymes that break down carcinogens. **Conclusion:** TD root extract will be a conventional medicine for rejuvenating and nephrogenic remedies, and shows promising chemopreventive efficacy in DMBA-induced HBPs Cancer.

Keywords: Oral cancer, *Trianthema decandra*, DMBA, Cisplatin, Antioxidant, LPO.

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INTRODUCTION

Cancer begins with a multi-step process strongly influenced by a genetic flaw and exposure to caustic external factors. The most widespread malignant tumour in the head and neck region is oral cancer.[1] The oral cavity-based malignant tissue goes through three stages of commencement, promotion, development, and growth. More than 90% of all malignancies are caused by oral cancer, which makes it the sixth most prevalent type of cancer internationally. Approximately 211,000 people across the globe die from oral cancer each year, and 405,000 new instances have been reported. It ranks among the top cancers, responsible for fatalities in South Asian nations.[2] The multiple steps involved in the development of cancer are caused by a genetic mutation. The main causes of the higher occurrence in India are drinking alcohol, smoking cigarettes, and chewing betel nuts with or without tobacco.[3]

Since the expansion of DMBA-induced oral carcinoma in HBP induces A great deal of the histological, biochemical, and cellular changes in human oral cancer, HBPCs is a proof model to study OC. DMBA is a strong pro-carcinogen with organ- and site-specificity.[4]

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Phase I enzymes should convert this carcinogen into Diol epoxides, reactive compounds that can attach to the DNA and encourage the growth of cancer cells. Phase II conjugating enzymes detoxify reactive metabolites into inactive metabolites and expel them. Reactive metabolites are created during the metabolic activation of DMBA.[5]

Dietary components have developed into a promising method of cancer prevention called chemoprevention. It is anticipated that many plant-based chemotherapy preventative drugs would demonstrate their anti-tumor effects by inhibiting cell proliferation and promoting cell death. A significant resource for the investigation of therapeutically useful chemicals is medicinal plants. Due to their low toxicity and excellent tolerance, the aid of plant-derived antioxidants as chemopreventives is expected to be approved in clinical trials. There are 20 species in the genus *Trianthema*, although only a few have been studied for their phytochemical content. Indian origins of three species' phytochemical traits are known. Only a few compounds from the genus *Trianthema* have had their structures determined, including trianthenol, flavonoid and ketone while Neolignan and Ecdysteroids were recovered from *T. turgidifolia*. *Trianthema decandra* and its species are utilized for anti-inflammatory, anti-hyperglycemic, hepatoprotective, and antioxidant purposes in traditional medical systems like Ayurveda and Unani. There are numerous phytochemicals from this genus, but not from this species, that have been identified, including terpenoids, alkaloids, and flavanoids. Studies on *Trianthema decandra* have revealed that the extract has pharmacological effects.[6]

By examining TD extract modulating effect on determination of LPO by-products (TBARS, LOOH, and CD), enzymatic antioxidants (SOD, CAT, and GPx), non-enzymatic antioxidants (Vit-E and GSH), renal markers (BUN and creatinine) histopathological pattern, and using ELIZA to analyze the apoptotic markers caspase-3 and 9, it has been found that the extract exhibits an adapting impact on the molecular markers that regulate cell proliferation and apoptosis' expression variations.[7]

MATERIALS AND METHODS

Making solvent extracts using soxhalation

A sample of 200 g of shade-dried root powder was taken in a thimble, and ethanol followed by chloroform was used to extract the samples. The filtrate was then concentrated using the rotary evaporator (Buchi R200 Rota vapour). Collection, labelling, and storage of the sample at 4°C in a refrigerator were completed.

Experimental design – I (dose-dependent study)

All animal quarantine and experimental procedures Figure 1 was conducted based on the Purpose of CPCSEA (proposal no IAEC/M.PORKODI/AU/Ph.D/KMCP/160/2022-23) as well as according to the guidelines established by the Ministry of Environment, Forests, and Climate Change of India's committee for 48 Syrian golden hamsters weighing 80g to120g to be procured from Biogen, Animal Laboratory House and maintained in Central Animal House, K M College of Pharmacy, Madurai. They will be acclimatized for 1 week prior to the experiment and then randomly divided into six sets of animals with eight animals in each set. Hamsters from group 1 were used as an untreated control group (Vehicle Control (Carboxy Methyl Cellulose). Using a no. 4 brush, 0.5% DMBA in liquid paraffin was applied to the left HBP of group 2-5 hamsters 3 times/week for twelve weeks. Animals in group 2 often further received a standard pellet diet only. Additionally, hamsters in groups 3 (200 mg/kg bw po), and 4 (400 mg/kg bw po) TD extract received orally three times per week via intragastric tube beginning starting days one week before being exposed to the carcinogen and alternated with the DMBA painting for 12 weeks, and group 5 (7.5 mg/kg b.w, ip) injected with cisplatin at the end of 12 weeks for 7 days. Group 6 was TD extract (400 mg/ kg b.w po for 12 weeks) alone treated hamsters.

The animals were sacrificed under harmless anaesthesia 24 hr afterwards their last treatment using ketamine. Blood samples were collected through intra orbital sinus puncture from each hamster and centrifuged for 15 min at 3000 rpm after that the blood to clot at 35°C for 30 min. The serum sample was collected and stored at -20°C for biochemical studies. Liver, Kidney and buccal pouches tissues were dissected and processed for the preparation and homogenate and histological studies. To determine the animal's body weight; the starting and final weights were subtracted. It was determined how many tumors there were overall in the HBP. The number of tumours per hamster was multiplied by the tumour volume to determine the tumour burden. Thus, we found 200 mg/kg b.w. as the efficacious dose for the chemoprevention investigation related to molecular experiments.

Biochemical analysis

Sample collection

Samples of blood and buccal mucosa were taken from each group's experimental and control hamsters

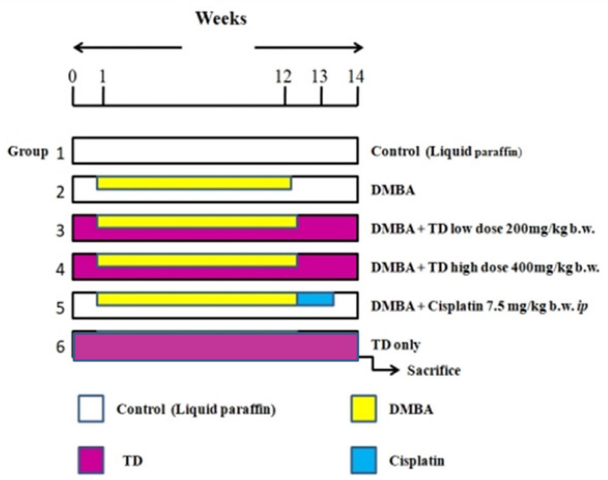

Figure 1: Schematic illustration of the experimental design.
DMBA, 7, 12-dimethylbenz (a) anthracene, TD-*Trianthema decandra* Root Extract.

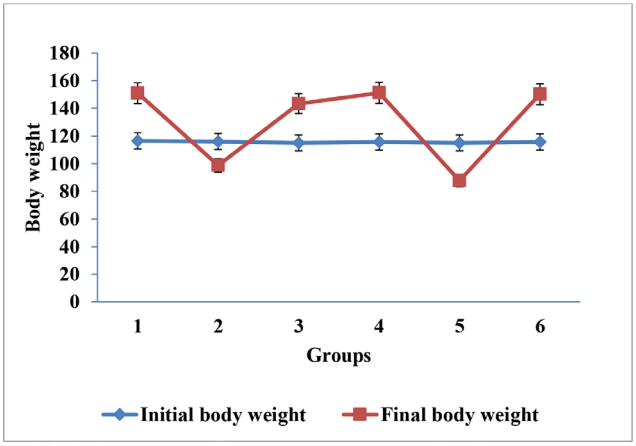

Figure 2: The body weight of untreated control and experimental hamsters.
Values are expressed as mean ± SD for six hamsters in each group. Values not sharing a common superscript letter differ significantly at p <0.05 (DMRT).

were studied biochemically. Heparinized tubes were helped to collect blood samples. Centrifugation was used to separate the plasma for 15 min at 1000g. To perform biochemical calculations, tissue samples were homogenized in an Using a Teflon pestle after being cleaned with ice-cold saline and the required buffer, an all-glass homogenizer was used.

The protein content by Lowry *et al.* technique. The quantification methodology was used to quantify CD, LOOH and TBARS, respectively.[8-10] The activity of SOD, GPx, and CAT were measured using methods created by respectively.[11-13] Using methods outlined by respectively,[14,15] the levels of Vit-E and GSH in the plasma and buccal mucosa were measured, BUN was estimated,[16] whereas serum creatinine was determined by the alkaline picrate methods.

Enzyme-linked immunosorbent assay (ELISA) estimation of caspase-3 and 9 activities

The apoptotic marker enzymes caspase-3 and 9 have been examined in the buccal mucosa using the ELISA assay kit. The findings are supported by the spectrophotometric detection of the chromophore pNA, which is detected at 405 nm using a microplate reader as the result of the cleavage of the labelled substrates caspase-3 substrate DEVD pNA and caspase-9 substrate LEHD-pNA.

Statistical analysis

In SPSS version 17.0 for Windows, the data were compared using one-way Analysis of Variance (ANOVA) and Duncan's Multiple Range Test (DMRT). Data is presented as mean SD. (SPSS Inc., Chicago, IL).

RESULTS

Effect of TD extracts on body weight changes

The differences in body weight measurements were noted every week of experimental rats are shown in Figure 2 at the beginning and end of each stage. In comparison to group 1 hamsters, the level of body weight was considerably (p<0.05) lower in group 2 hamsters. For DMBA-painted hamsters, oral TD extract administration at various doses of 200, 400 mg/kg b.w. and Cisplatin 7.5mg/kg/bw resulted in an increase in body weight that was substantial (p<0.05). Hamsters treated with TD extract (200 and 400 mg/kg b.w.) showed appreciable gains in body weight.

Effect of TD extract on tumor burden, incidence, and Volume

Table 1 described hamsters painted with DMBA alone, we saw 100% tumour formation with mean tumour volume (175.05 mm^3) and tumour burden (1575.45 mm^3) (group 2). In DMBA-treated hamsters, oral TD extract and cisplatin given to groups 3, 4, and 5 extensively (p< 0.05) reduced the occurrence, volume, and burden of tumours respectively. In control and drug-alone hamsters, no tumour was seen (Groups 1 and 6) respectively. Because of this, the action of TD extract at dosages of 200 and 400 mg/kg bw has noticeable impacts on DMBA hamsters.

Estimation of LPO

Figures 3 and 4 indicate the LPO marker amounts (TBARS, CD, and LOOH) in the buccal mucosa and plasma of experimental and control hamsters. When

Table 1: Tumor incidence, number, volume and burden of experimental hamsters.

Groups/ Treatment	Control	DMBA	DMBA + TD (200 mg/kg bw)	DMBA + TD (400 mg/kg bw)	DMBA + Cisplatin (7.5 mg/kg bw)	TD Alone (400 mg/kg bw)
Tumor incidence	0	100%	0	0	0	0
Total number of tumor/hamsters	0	9 ± 0.69	0	0	0	0
Total volume (mm^3)/hamsters	0	175.05 ± 13.41	0	0	0	0
Tumor burden (mm^3)/hamsters	0	1575.45 ± 120.65	0	0	0	0

Values are expressed as mean ± SD for six hamsters in each group. Values not sharing a common superscript letter differ significantly at $p < 0.05$.

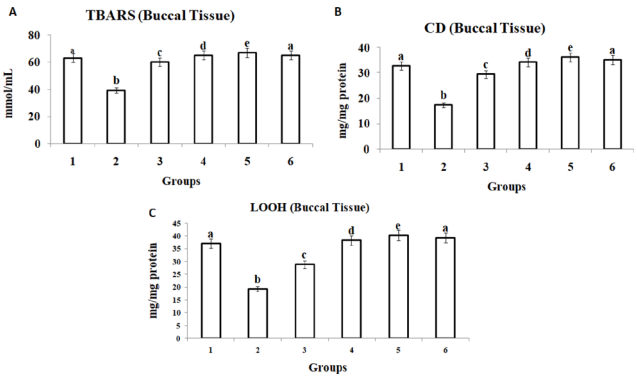

Figure 3: Status of LPO (TBARS, CD and LOOH) levels in Buccal mucosa in control and experimental hamsters in each group.

Bars are expressed as mean SD for 6 animals in each group. (a–e) Values that do not share a common superscript letter between groups different significance. b significantly different from group 1 at $p< 0.01$; c significantly different from group 1; c significantly different from group 1 at $p< 0.001$; d significantly different from group 1 at $p< 0.05$; e significantly different from group 1 at $p< 0.05$ (DMRT).

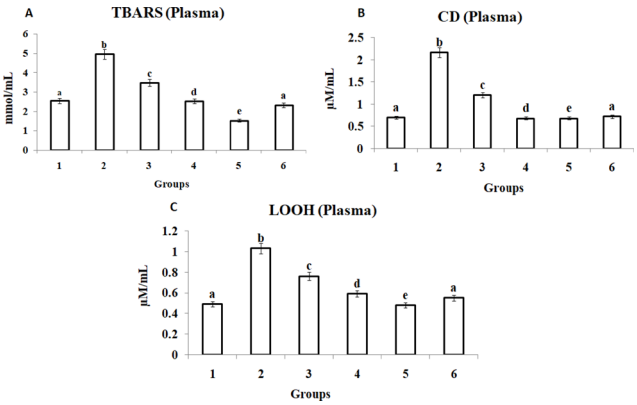

Figure 4: Status of LPO (TBARS, CD and LOOH) levels in Plasma of control and experimental hamsters in each group.

Bars are expressed as mean SD for 6 animals in each group. (a–e) Values that do not share a common superscript letter between groups different significance. b significantly different from group 1 at $p< 0.01$; c significantly different from group 1; c significantly different from group 1 at $p< 0.001$; d significantly different from group 1 at $p< 0.05$; e significantly different from group 1 at $p< 0.05$ (DMRT).

compared to LPO by-product levels were considerably ($p<0.05$) higher in the blood sample and lower in the considering the buccal tissues of DMBA and control hamsters (group 2). In comparison to Group 1, plasma and buccal mucosa levels of LPO by-products were considerably (p 0.05) recovered by 200 and 400 mg/kg bw of TD extract administered orally and Cisplatin at 7.5 mg/kg bw. In the control hamsters (groups 1 and 6), no significant change was found.

Enzymatic antioxidants tests

Figures 5 and 6 is the buccal and Plasma of each group of experimental and control hamsters that were examined for the presence of enzyme antioxidants (SOD, CAT, and GPx). The plasma and buccal mucosa enzymatic antioxidant content in the hamsters administered DMBA alone was noticeably (p 0.05) lower, with the exception of GPx (which increased) (group 2). When oral doses of TD extract at 200 and 400 mg/kg bw and Cisplatin at 7.5 mg/kg bw were administered to DMBA-treated hamsters in groups 3, 4, and 5, current tests were considerably ($p< 0.05$) returned to practically normal compared to group 1 and 6.

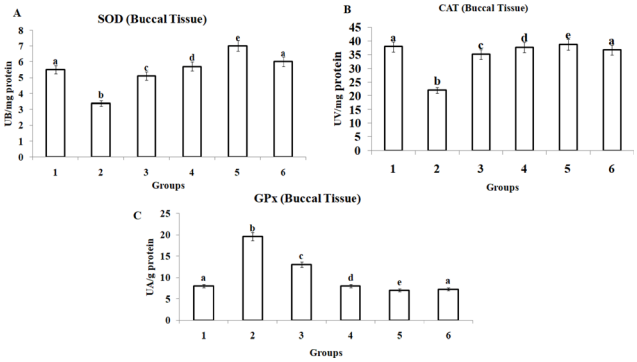

Figure 5: Status of Buccal tissue enzymatic antioxidants in control and experimental hamsters in each group.

Bars are expressed as mean SD for 6 animals in each group. (a–e) Values that do not share a common superscript letter between groups different significance. b significantly different from group 1 at $p< 0.01$; c significantly different from group 1; c significantly different from group 1 at $p< 0.001$; d significantly different from group 1 at $p < 0.05$; e significantly different from group 1 at $p<0.05$ (DMRT). A – Micromoles of glutathione utilized/minute; B – The number of enzymes required to inhibit 50% Nitroblue-Tetrazolium (NBT) reduction; C – Micromoles of H2O2 utilized/s.

Non-enzymatic antioxidants tests

Figure 7 shows the concentrations of non-enzymatic antioxidants (Vitamin E and GSH) in the plasma and buccal mucosa of each group of control and

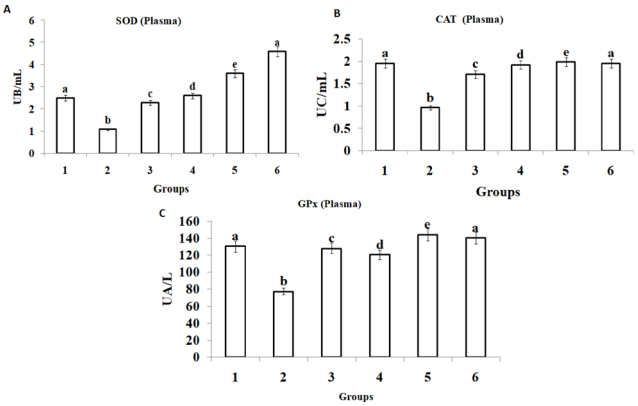

Figure 6: Status of plasma enzymatic antioxidants in control and experimental hamsters in each group.

Bars are expressed as mean SD for 6 animals in each group. (a–e) Values that do not share a common superscript letter between groups different significance. b significantly different from group 1 at $p< 0.01$; c significantly different from group 1; c significantly different from group 1 at $p< 0.001$; d significantly different from group 1 at $p < 0.05$; e significantly different from group 1 at $p<0.05$ (DMRT). A – Micromoles of glutathione utilized/minute; B – The number of enzymes required to inhibit 50% Nitroblue-Tetrazolium (NBT) reduction; C – Micromoles of H_2O_2 utilized/s. Thiobarbuturic Acid Reactive Substances (TBARS).

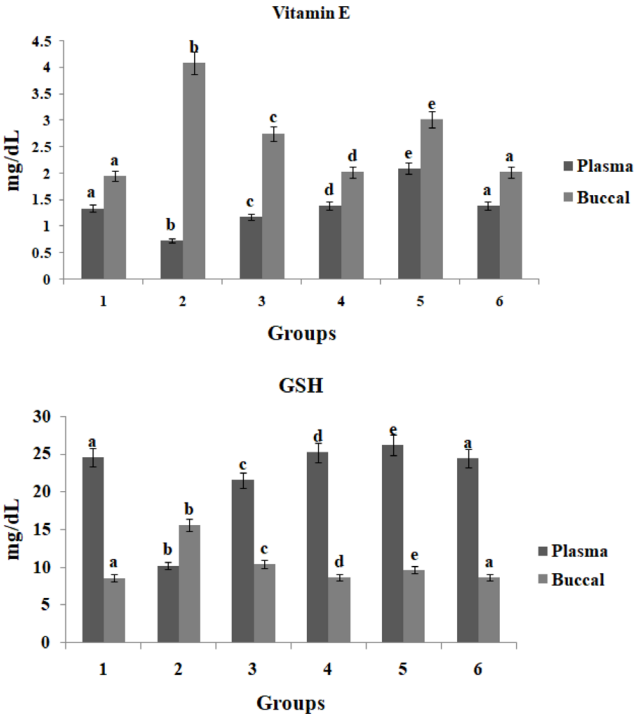

Figure 7: Status of plasma and buccal mucosa non-enzymatic antioxidants in control and experimental hamsters in each group.

Bars are expressed as mean SD for 6 animals in each group. (a–e) Values that do not share a common superscript letter between groups different significance. b significantly different from group 1 at $p< 0.01$; c significantly different from group 1; c significantly different from group 1 at $p< 0.001$; d significantly different from group 1 at $p< 0.05$; e significantly different from group 1 at $p< 0.05$ (DMRT).

experimental hamsters. Plasma non-enzymatic antioxidant levels significantly (p 0.05) reduced, although they increased in the buccal mucosa of the hamsters in group 2 who received DMBA alone. dosages of 200 and

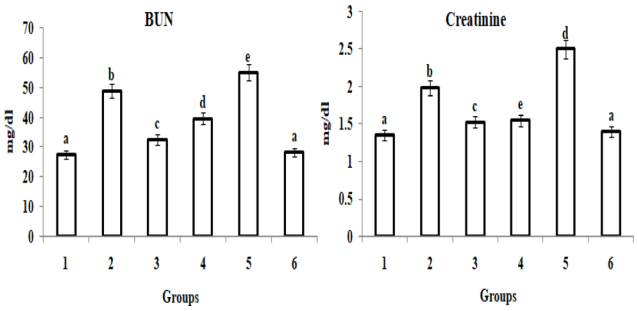

Figure 8: Status of kidney function markers BUN, serum creatinine in control, and experimental hamsters in each group.

Values are given as mean ± SD from six hamsters in each group. Values that do not share a common superscript letter between groups different significance. b significantly different from group 1 at $p< 0.01$; c significantly different from group 1; c significantly different from group 1 at $p< 0.001$; d significantly different from group 1 at $p< 0.05$; e significantly different from group 1 at $p< 0.05$ (DMRT). BUN, blood urea nitrogen; DMBA, 7, 12-dimethylbenz (a)anthracene; TD-*Trianthema decantra* extract.

400 mg/kg bw of TD extract and compared to groups 1 and 6, giving cisplatin at a pre-treatment dose of 7.5 mg/kg body weight Both the buccal mucosa and plasma of hamsters treated with DMBA significantly (p 0.05) recovered from non-enzymatic antioxidant status.

Effect of TD on renal function marker

Figure 8 shows the plasma concentrations of BUN and Creatinine in Serum (SC) were predicted in experimental and control hamsters. Increased BUN and SC levels were observed in Group 5 (DMBA + cisplatin 7.5 mg/kg bw, ip) as compared to Group 1 (p 0.05). In comparison to the control, Group 2 had significantly higher BUN and SC levels (p 0.05). Hamsters in Groups 3 and 4 who received TD demonstrated normal BUN and SC levels when compared to Group 1 (p 0.05).

TD impact on the buccal mucosa's histological alterations

Table 2 (Groups 1-6) shows the results of buccal mucosa tissues from control and trail hamsters that have been analysed histologically. Group 1 hamsters showed the expected cellular structure and no signs of abnormal cell development. The well-differentiated SCC with malignant tumour infiltration with Hamsters in group 2 had a few neutrophils near the keratin pearls. The mucosa of the buccal cavity of the treated hamsters in Groups 3 and 4 showed considerable hyperplasia, moderate keratosis, and mild dysplasia. The hamsters in group 6 had normal cellular architecture but in group 5 showed modest hyperplasia and moderate hyperkeratosis of the squamous epithelium.

Table 2: Histopathological changes in the buccal mucosa of experimental hamsters.

Groups/ Treatment	Control	DMBA	DMBA + TD (200 mg/kg bw)	DMBA + TD (400 mg/kg bw)	DMBA + Cisplatin (7.5 mg/kg bw)	TD Alone (400 mg/kg bw)
Keratosis	0	+++	++	++	+++	-
Hyperplasia	0	+++	+	+	+++	-
Dysplasia	0	+++	+	-	++	-
OSCC	0	+++	-	-	+	-

- = No change, + = Mild, ++ = Moderate, +++ = Severe.

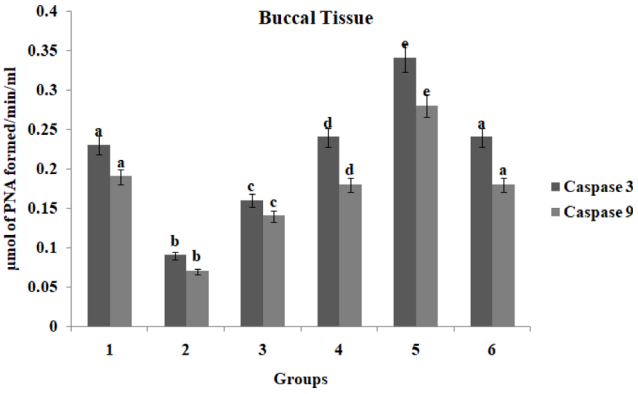

Figure 9: Status of Caspase 3 and 9 activities in the buccal mucosa of untreated control and experimental hamsters.

Bars are expressed as mean ± SD for six animals in each group. Values not sharing a common superscript differ significantly at $p < .05$ (Analysis of variance followed by DMRT).

Analysis of apoptotic markers in buccal region tissue by ELISA

The apoptotic markers enzymes caspase-3 and caspase-9 in experimental and untreated hamster buccal mucosa as seen in Figure 9. In group 2 tumor-bearing hamsters, the caspase-3 and caspase-9 reactions were significantly ($p \leq 0.05$) diminished. When compared to group 2, oral TD extract treatment in hamsters painted with DMBA (group 3), the status of the aforementioned markers was noticeably ($p \leq 0.05$) shifted towards the usual range. When hamsters treated with groups 3, 4 and 5 were compared to hamsters treated with groups 1 and 6, there was no discernible variation in the status of the aforementioned markers.

DISCUSSION

Chemotherapy, radiation therapy, and surgery are among the therapeutic modalities used to treat cancer worldwide; nevertheless, these treatments are typically accompanied by serious adverse effects. Natural substances, especially those derived from plants, are being researched for their potential to fight cancer and have shown the ability to recognise the molecular targets of the disease. Natural or biological medicines can halt the spread of cancer through a process known as cancer chemotherapy.

Trianthema decandra Linn., a family of Aizoaceae, also TD known as gadabani in Hindi and vellaisharuni in Tamil. TD is a prostrate herb that grows in tropical and subtropical climates all over the world. TD is also widely distributed in India. TD has been accepted by various traditional medical systems for the treatment of human diseases and afflictions.[17] TD has been used for treating a variety of illnesses since ancient times, including burns and wounds, numerous infectious diseases and bacterial infections, fever, toothaches, hepatoprotective, analgesic, anti-inflammatory, antidiabetic, and other skin disorders.[18] TD is also known to have curative properties. TD and its species are utilised for anti-inflammatory, anti-hyperglycemic, hepatoprotective, and antioxidant purposes in traditional medical systems like Ayurveda and Unani.[19]

The chemotherapy drug cisplatin based on platinum and is used to treat a multitude of malignancies, has grave side effects which include gastrointestinal toxicity, ototoxicity, neurotoxicity, and especially nephrotoxicity. According to clinical tests, cisplatin-induced nephrotoxicity may result in a decrease in glomerular filtration rate and an increase in the blood levels of creatinine and urea nitrogen.[20] Cisplatin is the most widely prescribed cell-killing anticancer drug for the treatment of oral cancer. Cellular DNA experiences anticancer effects thanks to cisplatin. Damage, replication errors, transcriptional inhibition, and cell cycle arrest all lead to apoptosis.

The main duties of the kidneys consist of drug metabolism and excretion via exogenously produced therapeutic and diagnostic compounds. A well-known renal adverse effect of most treatments for cancer is renal tubular trauma. Due to the quick blood flow, massive amounts of circulating pro-inflammatory cytokines are instantly exposed to the kidney.

Furthermore, cytokines and chemokines can be manufactured by the kidneys' tubular epithelium and distributed by the kidneys.[20] As a result, the kidney is exposed to responses to inflammation, therefore greatly leading to the degradation of renal continue to operate.[21-23] Creatinine levels in the circulatory system increase as an indicator of impaired renal function.

Atypically excessive levels of creatinine are a sign suggesting. The kidneys can be declining or failing. The BUN level is yet another sign of healthy kidneys.

If renal function is compromised, the metabolic waste product urea may build up. Cisplatin concentrations in the blood and kidney are roughly five times higher than they are in the serum of proximal tubular epithelial cells.[24,25] It represents an accumulation of renal parenchymal cells.[26] SC and BUN are the functional nephrotoxic markers used to identify the underlying cause of renal failure.[27] According to earlier investigations, the levels of renal function warning signs significantly increased as a result of cisplatin-induced nephrotoxicity.[25]

BUN and SC levels in the tumor-bearing hamsters used in our investigation were discovered to be noticeably elevated. We were able to confirm the early stages of nephrotoxicity in Group 5 hamsters treated with cisplatin as a result. The nephroprotective behaviour of TD root extract in addition to its chemo-preventive properties can now be compared in hamsters treated with cisplatin and treated with TD root extract. The preventative administration of TD root extract to cisplatin reduces the inflammatory response thought to be responsible for the medication-induced acute damage to the renal system during DMBA-induced HBC. It might be useful as an add-on to chemotherapy for cancer, which already uses cisplatin treatment. Understanding the potential for cancer prevention in pharmacologically active natural and developed drug medicines has been a key focus of contemporary research on cancer chemoprevention. Cancer remains at 50% because oral cancer is frequently found in its early stages. The most extensively used animal model of experimental oral cancer is DMBA-induced HBPCs, and using this model could assist in determining whether a test substance is effective at preventing cancer before beginning clinical trials.[28]

This study looked into the ability of TD root extract to inhibit DMBA-induced mouth carcinogenesis. When compared to control hamsters, hamsters DMBA only painted during 14 weeks displayed significant histopathological and biochemical abnormalities and also, we saw 100% development of the tumour, and the cancer was well-differentiated squamous cell carcinoma, as revealed by pathology. The seriousness of early-cancerous lesions such as hyperplasia, hyperkeratosis, and dysplasia has been evaluated via oral pathologic research.[29]

In hamsters given DMBA alone, we observed significant hyperplasia, hyperkeratosis, and dysplasia. The development of tumours in the hamsters DMBA only painted was totally avoided treated TD root extract at a dose of 200mg/kg bw. However, we observed moderate dysplasia and hyperplasia in the DMBA+ TD extract-treated hamsters, which was likely brought on by the 14-week period of mechanical irritation from the brush.[30] The 100% suppression of tumour formation in DMBA-treated hamsters' buccal mucosa shows that TD root extract repressed aberrant proliferation in DMBA-induced HBPCs.

Phase II enzymes were in the potential role of detoxification of synthetic carcinogens, whereas phase I biotransformation substances participated in the metabolic activation of carcinogens.[31] Experimental studies show that photochemical decreases phase I enzyme activity to halt the biotransformation of DMBA. Numerous ingredients from medicinal plants could appear to be phase I enzyme inhibitors. According to research, phase I and phase II enzyme activity was significantly altered by DMBA-induced HBPCs. Our findings corroborate these conclusions. The livers of DMBA-treated hamsters displayed increased phase I enzyme activity and decreased phase II enzyme activity, demonstrating that DMBA-induced HBPCs led to the deposition rather than clearance of dihydrodiolepoxide, the compound's most cancer-causing metabolite. It is likely that low glutathione availability contributed to the lower GST and GR activity in the liver of hamsters administered DMBA since glutathione is necessary for the detoxification of cancer-causing substances and the scavenging of ROS.[32]

According, inappropriate clearance of ROS causes a number of clinical diseases, including cancer. Accordingly, ROS have a role in the invasion and metastatic stages of carcinogenesis. Oral cancer has been linked due to the insufficient availability of an LPO substrate called polyunsaturated fatty acids.[33] Low levels of LPO by products are seen in rapidly growing tumour cells. Oral cancer diminished LPO with alterations in the antioxidant status have been widely reported. Our research confirms these conclusions. Cancer tissues have higher GPx activity and GSH levels, which suggests that these molecules control cell proliferation.[34] SOD and CAT activity reductions have been observed in tumour tissues from a variety of malignancies, including oral cancer. Our research supports these viewpoints.

By halting the harmful effects of ROS, antioxidants are essential in the defence of human health. Antioxidants, both enzymatic and nonenzymatic, actively scavenge ROS and shield cells from oxidative DNA damage induced through ROS. SOD is thought to catalyse the transformation of hydrogen peroxide and atomic oxygen via superoxide anion. According to, CAT catalyses the conversion of hydrogen peroxides into

water and molecular oxygen.[35] By catalysing the reduction of hydroperoxides, GPx shields the cell from oxidative damage along with its cosubstrate GSH. Studies have shown that the bioactive components of natural products suppress the development of cancer by reducing the amount of LPO caused by free radicals and by boosting the antioxidant defence mechanism.

To meet their dietary needs and for their accelerated growth, tumour antioxidants and nutrients are stowed away by cells from the bloodstream. The LPO process can spread to different tissues when LPO are produced at the primary site. Increased plasma TBARS levels in DMBA-treated hamsters are likely caused by ROS buildup or not enough and poor production of antioxidant potential. As a result of scavenging the system's excessively created ROS, antioxidants, both enzymatic and nonenzymatic, lose energy, which results in reduced levels of both.[36] TD root extract was given orally to hamsters who had been given DMBA to improve their plasma LPO and antioxidant status. According to our findings, TD root extract inhibited the build-up of ROS in hamsters given DMBA treatment by non-enzymatic antioxidant concentrations and the increased activity of antioxidant enzymes.

An improvement in the antioxidant defence system may have boosted the functions of the detoxifying process in hamsters treated with DMBA+ TD root extract, limiting the metabolic activation of DMBA. It has been suggested that TD root extract plays a powerful and multifaceted antioxidant role.[37]

Nitric Oxide (NO), superoxide, and hydroxide radicals were all quenched by TD root extract. TD root extract's ability to inhibit LPO has been well established. According to studies, TD root extract has a potent effect on quenching superoxide anion radicals. According to TD root extract improved cell viability and protected against oxidative damage brought on by NO, O2, and ONOO *in vitro*.

TD root extract antioxidant capacity has also been linked to other pathways, including the elimination of oxygen Scavenging of nitrogen species and ROS, or their precursors.[38] Nitrogen and reactive oxygen species are blocked, and the metal ions needed to catalyse the synthesis of reactive oxygen are bound, and endogenous antioxidant defences are activated. The equilibrium during DMBA-induced oral carcinogenesis, oxidant and antioxidant states is maintained by TD root extract, according to our findings, which decreased DMBA-induced oxidative stress. Thus, our study illustrated how TD root extract protects hamsters given DMBA treatment from oxidative stress.[39]

CONCLUSION

The findings of this investigation indicate that TD root extract has the power to halt or inhibit the early stages of oral carcinogenesis. TD root extract was shown to have chemo-preventive capacity in DMBA-induced HBPCs. The therapeutic potential of TD root extract is probably due to its antioxidant properties, its calming effect on the detoxification process, and the fact that it allows the kidneys to control blood serum levels of creatinine and urea nitrogen during DMBA-induced oral cancer. This study is being expanded to look at the impact of TD root extract on the regulation of several molecular markers linked to oral carcinogenesis to further establish the efficacy of TD root extract.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

ABBREVIATIONS

DMBA: Dimethylbenzaanthracene; **HBPs:** Hamster Buccal Pouch Carcinogenesis; **TD:** *Trianthema decandra*; **LPO:** Lipid Per oxidation; **SOD:** Superoxide dismutase; **TBARS:** Thiobarbutric acid reactive substances; **LOOH:** Lipid peroxides; **CD:** Conjugated Dienens; **CAT:** Catalase; **GPx:** Gluthathione Peroxidase; **Vit E:** Vitamin E; **GSH:** Glutathione; **BUN:** Blood Urea Nitrogen; **CPCSEA:** Control and Supervision of Experiments on Animals; **pNA:** p-Nitroaniline.

SUMMARY

Altogether TD root extract has a potent therapeutic effect due to its antioxidant properties, its calming effect on the detoxification process, and the fact that it allowed the kidneys to control blood serum levels of creatinine and urea nitrogen against cisplatin exposure on DMBA-induced oral cancer. Further establishing the effectiveness of TD root extract, this study is being expanded to examine the effects of TD root extract on the regulation of multiple molecular markers associated with oral carcinogenesis.

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