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Reversal of deltamethrin-induced oxidative damage in rat neural tissues by *turmeric-diet*: Fourier transform-infrared and biochemical investigation

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Turmeric-diet

Abstract The present study is designed to determine the protective effect of turmeric (TMR) against neural oxidative damage caused by deltamethrin (DLM). Here we have employed mainly Fourier transform-infrared (FT-IR) spectroscopy to understand this event, in addition to biochemical analysis. For this purpose, rats were randomly divided into four groups ($n = 6$); control, TMR (1% *turmeric-diet*), DLM-treated (41 ppm) and TMR co-administrated with DLM for 48 days. The FT-IR spectra of brain tissues reflect the significant changes in the area values of macromolecules including proteins, lipids and nucleic acids in DLM-treated rats compared to control. In addition, DLM caused increase in the malondialdehyde (MDA) level accompanied by decrease in antioxidant enzymes activity such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR). However, the TMR co-administered with DLM group, exhibits appreciable restoration in area values and peaks of IR spectra and also the restoration of the mentioned antioxidant enzyme activities. The group merely fed with TMR showed insignificant changes in all investigated parameters. Therefore, the results reveal that, 1% of turmeric has a protective effect against deltamethrin caused neural oxidative damage.

Introduction

For the sake of more food production and domestic pest control number of pesticides and insecticides have been used in the agricultural and non agricultural practices. Deltamethrin (DLM) (Fig. 1) is fast acting neurotoxic pyrethroid obtained from natural toxin pyrethrin (Aksakal et al., 2010; Guardiola et al., 2014; Mani et al., 2014). It is chemically designed to be more toxic to insects nervous system for the slow break down and formulated with synergists increasing potency and compromising the body's ability of detoxification (Thatheyus and Selvam, 2013; Haverinen and Vornanen, 2014). Lozowickaa et al. (2014) have reported that, the residues of DLM were detected on cereals at the range of 0.02–0.88 mg kg^{-1}. Owing to the extensive use of pyrethroids in agriculture and domestic activities, there are more chances of

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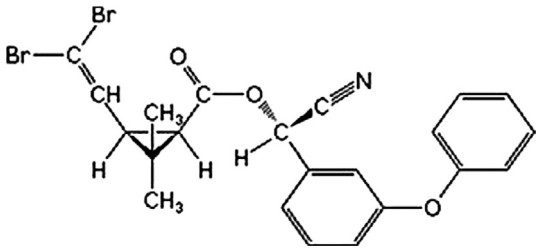

Fig. 1 Molecular structure of deltamethrin.

exposure to these chemicals, leading to neurodegenerative diseases (Baltazar et al., 2014). Such exposures have been observed more frequently in developing countries (Rother, 2014).

Although, DLM exhibits, relatively low mammalian and avian toxicity (Haverinen and Vornanen, 2014). Several studies were demonstrated that DLM is one of the most neurotoxic pyrethroids to insect and mammals too (Shafer et al., 2005; Kim et al., 2006; Gullick et al., 2014; Olsvik et al., 2014). It makes conformal changes in the structure of α- and β-subunits of the sodium channels (Ding et al., 2004) which lead to delayed closure of ion channels, resulting in a slow influx of sodium, hence slow depolarization (Ding et al., 2004; Chinn and Narahashi, 1985). Consequently, Shafer et al. (2005) and Eriksson and Fredriksson (1991) have reported that DLM is potential neurotoxicant, particularly in developmental stages of infants and children. Poisoning of pyrethroid induces some neurotoxic symptoms which include hyperexcitation, convulsions, seizures, and paralysis in rats (Symington et al., 2007). DLM also causes cerebrovascular and neurodegenerative disorders in humans (Godin, 2007). Neurodegenerative disease caused by DLM was shown to be exerted through oxidative stress (Hossain et al., 2005). It enhances the production of reactive oxygen species (ROS), including superoxide anion ($O_2^{\cdot-}$), hydrogen peroxide (H_2O_2) and hydroxyl radical ($^{\cdot}OH$) thereby causing DNA damage in rats (Roszczenko et al., 2013; Abdul-Hamid and Salah, 2013).

Indeed body has its own endogenous antioxidant mechanism to scavenge the produced ROS in the metabolism. However, the brain is an important, vital and delicate organ having more demand for oxygen and contains relatively low antioxidant enzymes. Studies demonstrated that, DLM induces oxidative stress in functionally different tissues. It is evidenced by increased MDA level, accompanied by the simultaneous decrease in the levels of antioxidant enzymes, including SOD, CAT, GPx and GR (Mazmanc et al., 2011; Shivanoor and David, 2014). The SOD converts $O_2^{\cdot-}$ into H_2O_2, further, H_2O_2 metabolism by peroxidases that include CAT and GPx yields H_2O (Wilcox, 2002). In addition to this, GPx plays a major role in the neutralization of H_2O_2, and OH to non-toxic products (Salvi et al., 2007). Thus, decreased activity of these enzymes may lead to an enhanced generation of ROS in the cells. Hence, measuring these enzyme activities and by-products of lipid and protein oxidation can provide evidence for oxidative damage (Ishrat et al., 2009). There are several investigations demonstrating that, the increased ROS causes oxidative damage to the macromolecules including proteins, lipids, carbohydrates and nucleic acids (Shivanoor and David, 2014; Bishnoi et al., 2008), consequently, oxidative stress in neural tissue leads to neurodegenerative diseases (Carloni et al., 2012).

In many situations exogenous antioxidant/s proved to reduce the damage caused by the ROS either by scavenging them or by enhancing the activity of endogenous antioxidant enzymes. Therefore, extensive research was carried out to find efficient natural herbal products to protect cells from damages caused by ROS. On the other hand use of phytochemicals as a therapy in diseases related to oxidative stress has gained immense interest for their ability to scavenge free radicals and their capability to protect body tissues against oxidative stress (Nabavi et al., 2012).

The herbal powder of *Curcuma longa* L. is well known as turmeric (TMR), has been traditionally used all over Asia to prepare curries and also as a preservative (Gilda et al., 2010; Prasad and Muralidhara, 2014; Mangolim et al., 2014). TMR has been used extensively as an effective therapeutic agent in an Ayurvedic and Chinese medicinal system (Sethi et al., 2009; Mendonça et al., 2013). Therefore, attention was paid on whole turmeric (*C. longa* L.), however curcumin is an active ingredient of turmeric, a naturally occurring phenolic phytochemical compound (Haiyee et al., 2009; Fu et al., 2014, 2015). It possesses anti-carcinogenic property in animal model (Yanyan and Zhang, 2014), anti-HIV (Fu et al., 2014) antioxidant (Yang et al., 2014), anti-inflammatory (Aggarwal et al., 2013; Antonyan et al., 2014) and anti-Alzheimer (Naksuriya et al., 2010 a). Curcumin has been reported to possess strong antioxidant properties that can inhibit the oxidative stress further the brain damage (Ataie et al., 2010; Samini et al., 2013). Recently, Yang et al. (2014) and Naksuriya et al. 2010 have reported that curcumin is found to be neuroprotective. There are few studies demonstrating that curcumin can be made effective and bioavailable by the *turmeric-diet* and also exhibits prevention to oxidative damage (El-Ashmawy et al., 2006; Martin et al., 2012). Furthermore, Thapliyal et al. (2002, 2003) and El-Shahat et al. (2012) found that *turmeric-diet* acts as an antioxidant by improving antioxidant enzyme activity in rat and mice.

In the present study, FT-IR spectroscopic technique was employed in addition to biochemical analysis; to evaluate the protective effect of TMR against the DLM caused oxidative damage in the brain. FT-IR spectroscopy is one of the vibrational spectroscopic techniques, which has been widely used as a quantitative and qualitative tool (Xiaonan et al., 2011; Ozek et al., 2014; Shivanoor and David, 2015) to detect and quantify the macromolecules in any biological samples (Xiaonan et al., 2011; Krishnakumar et al., 2012). Therefore, the present study uses this molecular fingerprinting approach in addition to biochemical analysis to investigate the protective effects of turmeric on DLM induced oxidative damage in rat brain tissues.

Materials and methods

Chemicals

Deltamethrin (Fig. 1)-DECIS 2.5 EC is an insecticide purchased from Bayer Pvt. Ltd, India. All other chemicals were of analytical grade, purchased from commercial vendors' in India.

Turmeric-diet

Turmeric power was obtained from Nani Agro Foods Pvt. Ltd. Tamil Nadu, India and prepared *turmeric-diet*. Proximate compositions of standard laboratory diet are presented in Table 1. However, 1% *turmeric-diet* was considered to be a therapeutic dose (El-Shahat et al., 2012; Reddy and Lokesh, 1994), it was prepared by thoroughly mixing 1 g of turmeric with 99 g of standard laboratory diet. This diet was prepared every week in the laboratory and stored at room temperature.

Experimental animals

Experiments were performed on Wister albino rats of approximately 150 ± 10 g body weight (BW). The animals were kept in plastic cages, the temperature (23 ± 2 °C), 12-h light/dark cycle with 60 ± 5% relative humidity were maintained in the animal house, Department of Zoology, Karnatak University, Dharwad. All animals were provided with standard laboratory diet (VLR, Mumbai) and *ad libitum* water. Animals were acclimatized for two weeks before the initiation of experiments and handled in accordance with the CPCSEA guidelines.

Experimental design

After acclimatization, rats were equally divided into the following four different groups.

Group I: Control; Rats (n = 6) were fed standard laboratory diet and received *ad-libitum* tap water throughout the experimental period.
Group II: Turmeric (TMR); Rats (n = 6) received *ad-libitum* tap water and fed *turmeric-diet* for 48 + 7 days.
Group III: Deltamethrin (DLM); Rats (n = 6) were fed on standard laboratory diet with simultaneous DLM exposure through water (41 ppm) for 48 days.
Group IV: DLM + TMR; Rats (n = 6) were fed *turmeric-diet* for 48 + 7 days and treated with DLM through water (41 ppm) for 48 days.

Sublethal dose of DLM (41 ppm) was equal to 1/12th of LD_{50}, 40 mg kg^{-1} BW (Aydin, 2011) was used in this study. DLM was given through the water because, it can completely dissolve and rapidly be absorbed in the gastrointestinal tract (Kim et al., 2006) and TMR was administrated with food because it's widely used in this approach. In the present study, TMR and DLM + TMR group rats were fed with *turmeric-diet* for 7 days before to start of DLM treatment and daily thereafter throughout the study for 48 days for acclimatization to *turmeric-diet* and it gives better protective results (Thapliyal et al., 2003).

Table 1 Composition of standard diet for rats.

Contents	Standard diet (%)
Moisture	6.00
Crude protein	18.40
Crude fat	4.35
Crude fibre	3.15
Calcium	1.10
Phosphorus	0.50
Total ash	4.50
Carbohydrates	62.00

Per kg of slandered diet provide 3140 kcal metabolizable energy to the rats. The *turmeric-diet* contains 1% turmeric herbal powder.

Sample preparation

Sampling and biochemical assays

Followed by the dissection brain was quickly removed, placed ice-cold normal saline solution and placed on ice and the whole brain was made into two parts right and left. For estimations of different oxidative stress related to biochemical parameters in the brain, 1 g of left half of brain tissue was minced into small pieces and homogenized in 10 mL of ice-cold phosphate buffer saline (PBS) (0.05 M, pH 7) to obtain 10% homogenate. The homogenate was centrifuged at 1500*g* and the supernatant was stored at −20 °C till further use. The right half of brain tissues were also immediately frozen in liquid nitrogen. Then minced and stored at −80 °C, further the tissues were dried in a lyophilizer (VIRTIS 6 KBEL 85) for 12 h to remove the water and the samples were used for the FT-IR analysis.

Brain biochemistry

Measurement of lipid peroxidation

Malondialdehyde (MDA), as a marker for lipid peroxidation, was determined by the double heating method of Draper and Hadley (1990). The Thiobarbituric acid (TBA) spectrophotometric assay was used. For this purpose, 2.5 mL of 10% (w/v) trichloroacetic acid (TCA) solution was added to 0.5 mL supernatant in a centrifuge tube and placed in a boiling water bath for 15 min and cooled, further the mixture was centrifuged at 600 *g* for 10 min, and 2 mL of the supernatant was transferred into a separate test tube containing 1 mL of 6.7 g l^{-1} TBA solution and placed again in a boiling water bath for 15 min for the reaction to complete. The solution was then cooled and the absorbance was measured at 532 nm. The molar extinction coefficient, 1.56×10^5 cm^2 $mmol^{-1}$ of malondialdehyde was used to calculate the malondialdehyde production and expressed as nmoles of MDA g^{-1} tissue.

Reduced glutathione (GSH)

The assay for GSH was determined by Ellman spectrophotometric method (1959), based on the development of a yellow colour when 5,5-dithiobis (2-nitrobenzoic acid) (DTNB) react with sulfhydryl groups. Briefly, 3 mL of 20% TCA and 1 mM Ethylenediaminetetraacetic acid (EDTA) was added to 0.5 mL of supernatant to precipitate the proteins. The mixture was kept at room temperature for 15 min, centrifuged at 2500*g* for 15 min at room temperature. The supernatant was used for the assay, the assay mixture contained 0.5 mL supernatant, 2.5 mL Ellman's reagent and was kept at room temperature for 20 min. The absorbance was read at 412 nm. The tissue glutathione level was calculated from the standard curve of known GSH concentration and expressed as mg g^{-1} tissue.

Determination of antioxidant enzymes activities

CAT activity was assayed spectrophotometrically by the decomposition of hydrogen peroxide (H_2O_2) according to the

method of Aebi (1984) and the enzyme activity was expressed as mmol H_2O_2 consumed min^{-1} mg^{-1} protein. SOD activity was evaluated following Kakkar et al. (1984) and the activity was expressed as U mg^{-1} of protein.

GP_X activity was measured according to Hafeman et al. (1973) and activity was expressed as nmoles of GSH oxidized min^{-1} mg^{-1} protein. GR activity was assayed by the method of Carlberg and Mannervik (1975) modified by Iqbal et al. (1998) and the enzyme activity was calculated as nmol NADPH oxidized min^{-1} mg^{-1} of protein.

Protein determination

Protein content in all tissue was determined according to Lowry et al. (1951) using BSA as a standard.

FT-IR analysis

Lyophilized tissue samples were ground in an agate mortar and pestle and made into a fine powder. Then powder sample was thoroughly mixed with completely dried IR grad potassium bromide (KBr) powder in the ratio 1:100 and dried again under a halogen lamp in order to remove any trace of water. Then all powered samples were subjected to a high pressure of 5 tonnes for 5 min to produce a clear transparent disc of 1 mm thickness. Finally, absorbance spectra of tissue samples pallets were recorded at room temperature (25 ± 1 °C) in the region ~4000–500 cm^{-1} on a Nicolet-6700 FT-IR spectrometer equipped with KBr beam splitter and an air cold deuterated triglycine sulphate (DTGS) detector. Each sample was scanned with three different pellets under identical conditions. These replicates were averaged and these averaged spectra for each sample were then used for further analysis. The spectra were analysed using Origin 8 software.

FT-IR second derivative analysis

The rat brain FT-IR spectra were composed of numbers of complex and overlapped peaks and to resolve these spectra the second derivative also used (Susi and Byler, 1986). The lipid band region (~3050–2800 cm^{-1}), amide-I band region (~1700–1600 cm^{-1}) was considered for the analysis of second derivative of the lipid and protein. The maxima in the FT-IR absorption spectra were minima in the second derivative.

Statistics

The data were analysed by using SPSS 16.0 for Windows. The significance of differences were calculated using ANOVA, followed by Tukey's or Students *t*-test for multiple comparisons. $P < 0.05$ was considered statistically significant.

Results

Effect of deltamethrin on brain MAD and GSH content

The changes in the tissue MDA level in different experimental groups represent (Fig. 2) there is a significant ($P < 0.001$) increase (42.05%) in the DLM treated group compared to control. There is a remarkable decrease in the MDA level which was observed when TMR is co-administrated with DLM (DLM + TMR) compared to the DLM treated group.

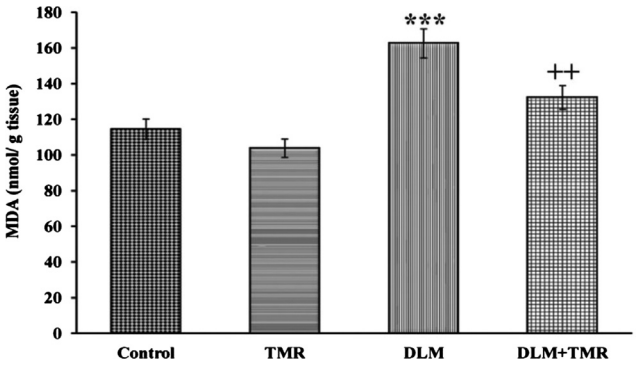

Fig. 2 Effect of TMR on DLM-induced alterations of MDA in rat brain. Values are mean ± SE for six rats in each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ for DLM alone treated group and merely feed *turmeric-diet* (TMR) groups vs. control and $^{+}P < 0.05$; $^{++}P < 0.01$ for (DLM + TMR) group vs. DLM alone treated group.

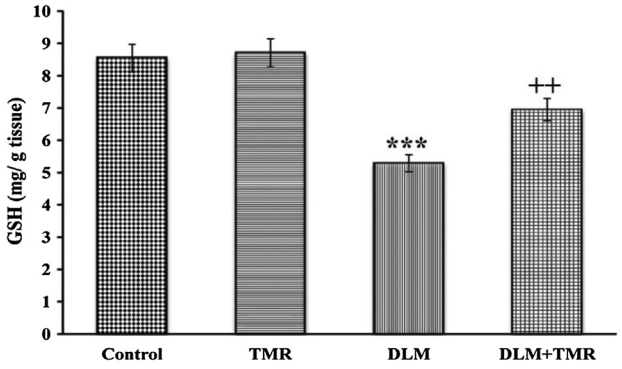

Fig. 3 Effect of TMR on DLM-induced alterations in the level of GSH in rat brain. Values are mean ± SE for six rats in each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ for DLM alone treated group and merely feed *turmeric-diet* (TMR) groups vs. control and $^{+}P < 0.05$; $^{++}P < 0.01$ for (DLM + TMR) group vs. DLM alone treated group.

The GSH level decreased by 38.12% ($P < 0.001$) in the DLM treated group compared to control (Fig. 3), while TMR co-administration with DLM, shows significant ($P < 0.05$) increase in the level of GSH when compared to DLM treated ones. In the present study the group merely fed on *turmeric-diet* (TMR) shows insignificant ($P > 0.05$) changes in MDA and GSH levels compared to control.

Antioxidant enzymes activities

The antioxidant enzyme activity has been represented in Table 2. SOD and CAT activity in brain tissues of DLM treated group were shown to be decreased significantly ($P < 0.001$) by 40.74% and 35.86% respectively, compared to control. Co-administration of TMR exhibits significant ($P < 0.05$) restoration in the activity of these two enzymes compared to DLM treated group. GPx activity was also inhibited significantly ($P < 0.001$) by 40.43% in the brain tissue after DLM treatment compared to control, while TMR co-administration with DLM (DLM + TMR) shows restoration

Table 2 Effect of turmeric (TMR) on deltamethrin (DLM) induced changes in the activity of brain antioxidant enzymes (SOD, CAT, GPx and GR).

Parameters	Experimental groups			
	Control	TRM	DLM	LTC + TRM
Catalase[a]	14.85 ± 1.23	15.16 ± 2.31	8.80 ± 1.36***	12.67 ± 2.43^{+}
Superoxide dismutase[b]	11.04 ± 0.83	11.42 ± 1.02	7.08 ± 0.54**	10.15 ± 0.46^{+}
Glutathione peroxidase[c]	32.58 ± 1.64	31.36 ± 1.2	20.48 ± 0.68***	25.71 ± 0.72^{++}
Glutathione reductase[d]	46.08 ± 1.17	47.08 ± 2.41	35.60 ± 1.16***	40.04 ± 1.06^{+}

Values are means ± SE for six rats in each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ for DLM and merely *turmeric-diet* feed (TMR) groups vs. control group and $^{+}P < 0.05$; $^{++}P < 0.01$: (DLM + TMR) group vs. DLM group.

[a] Catalase = μmmoles H_2O_2 degraded min^{-1} mg^{-1} protein.

[b] Superoxide dismutase = units mg^{-1} protein.

[c] Glutathione peroxidase = units mg^{-1} protein.

[d] Glutathione reductase = nmoles NADPH oxidized min^{-1} mg^{-1} protein.

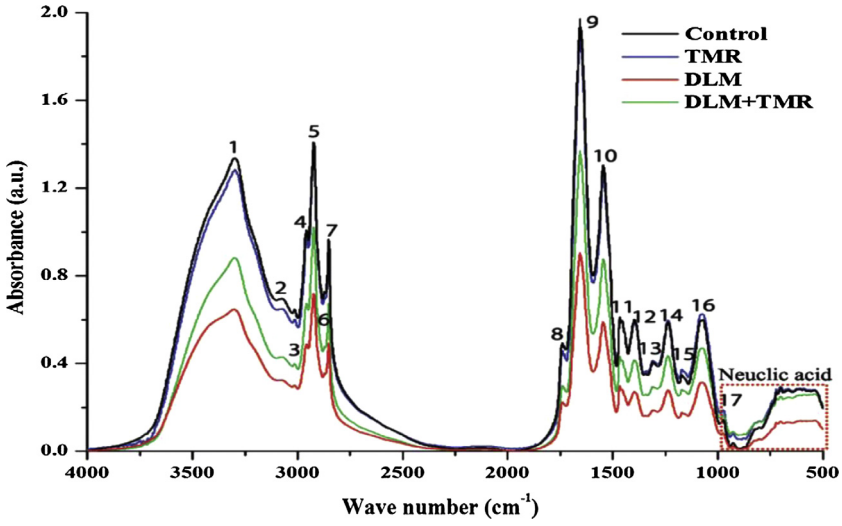

Fig. 4 The representative Fourier transform-infrared (FT-IR) spectra of rat brain tissues in the control., *turmeric-diet* (TMR)., deltamethrin (DLM) treated and TMR co-administrated with DLM (DLM + TMR) groups in the ~4000–500 cm^{-1} region.

in the GPx activity. The group treated with DLM, exhibits significant ($P < 0.001$) decrease in GR activity (22.74%) compared to control. The DLM + TMR group shows appreciable restoration in the GR activity, compared to DLM treated group, while the group merely fed on *turmeric-diet* (TMR) shows insignificant ($P > 0.05$) changes in all the antioxidant enzymes activity.

FT-IR analysis

The FT-IR absorption spectra between ~4000 cm^{-1} and ~500 cm^{-1} (Fig. 4) and the peak assignments (Table 3) shows, the changes in various macromolecules including lipids, proteins, polysaccharides and nucleic acids in control and treated groups. The detailed spectral analysis was performed in three distinct frequency ranges, namely ~3600–3050 cm^{-1} (Figs. 4 and 5), ~3050–2800 cm^{-1} (Figs. 4 and 6) and ~1800–800 cm^{-1} (Figs. 4 and 6) to know more details of the above said macromolecules. In addition to this, secondary derivative of the amide-I region (~1700–1600 cm^{-1}) and lipid region (~3050–2800 cm^{-1}) was analysed for protein and lipid secondary structure in the brain tissue (Fig. 6).

Fig. 5A mainly consists of amide-A vibrations of proteins in brain tissues range between ~3600 and 3050 cm^{-1}. The band appearing at ~3301 cm^{-1} in control was shifted to ~3297 cm^{-1} in the DLM treated group and ~3298 cm^{-1} in TMR co-administrated with DLM (DLM + TMR) group. Table 6 shows that there is a significant decrease (29.18%) in the ~3301 cm^{-1} band area in the DLM treated group compared to control. It reveals that the protein content in the brain tissues of DLM treated group is lesser than that of the control. While TMR co-administration with DLM (DLM + TMR) group shows significant ($P < 0.05$) increase in the corresponding area by 18.81% compared to DLM treated group, the group fed merely on *turmeric-diet* shows insignificant ($P > 0.05$) changes in the area values of this band compared to the control. The shoulder peak of amide-A was assigned to amide-B (Cakmak et al., 2006). The band appearing at ~3085 cm^{-1} in control was shifted to ~3073 cm^{-1} in the DLM treated group and the band area was significantly ($P < 0.01$) decreased by 28.54% compared to control, while TMR co-administrated with DLM reverse vibrational shifting in amide-B towards the control at ~3080 cm^{-1} and band area by 18.60% compared to DLM group. This result shows tur-

Table 3 General band assignments of the Fourier transform-infrared (FT-IR) of control, turmeric (TRM), deltamethrin (DLM) and TMR co-administered with DLM treated brain tissues based on the literature (Nabavi et al., 2012; Rother, 2014; Salvi et al., 2007; Samini et al., 2013; Sebnem et al., 2007).

Wave number in cm^{-1}					Vibrational peak assignments
Peak No	Control	TMR	DLM	DLM + TRM	
1	3301	3299	3297	3298	Amide-A: mainly N–H stretching of proteins with negligible contribution from O–H stretching of intermolecular hydrogen bonding
2	3085	3083	3073	3080	Amide-B: N–H stretching of proteins
3	3014	3015	3012	3014	Olefinic =C–H stretching: unsaturated lipids
4	2962	2961	2956	2960	CH_3 asymmetric stretching: mainly lipids
5	2927	2928	2923	2925	CH_2 asymmetric stretching: mainly lipids
6	2876	2876	2870	2874	CH_3 symmetric stretching: proteins
7	2856	2855	2852	2853	CH_2 symmetric stretching: lipids
8	1746	1743	1737	1739	Ester C=O stretching: lipids
9	1654	1655	1652	1653	Amide-I (protein C=O stretching)
10	1544	1543	1542	1543	Amide-II (protein N–H bend, C–N stretch)
11	1465	1465	1467	1467	CH_2 bending; lipids & proteins
12	1404	1406	1396	1401	COO– symmetric stretching: fatty acids
13	1307	1308	1305	1307	CH_3 CH_2 stretching: collagen
14	1242	1241	1236	1239	PO_2– asymmetric stretching: nucleic acids & phospholipids
15	1172	1170	1168	1170	CO–O–C stretching: glycogen
16	1075	1074	1072	1073	PO_2– asymmetric stretching: nucleic acids

meric administration that brought back the protein content in the brain tissue is correlated with protein estimated by Lowry et al. (1951) method for both (DLM + TMR) and control groups. The band at ~1544 cm^{-1} assigned to the amide-II protein in the brain tissue (Table 3). DLM treated caused significant ($P < 0.001$) decrease in the area of this band compared to control. TMR co-administration with DLM (DLM + TMR) brings back to the band area value towards the control values. In addition to this the results of calculated ratio of amide-II to amide-A protein showed significant ($P < 0.001$) increase in the DLM treated group compared to control (Table 6). TMR co-administrated with DLM (DLM + TMR) shows the restoration in the ratio towards the control, while the group fed merely on *turmeric-diet* showed insignificant ($P > 0.05$) changes in the both the amide bands, compared to control.

In order to investigate the changes in lipid content of rat brain tissues, the IR spectral region from ~3050 to ~2800 cm^{-1} was considered. In this region peaks arise from absorptions of olefinic (=CH), CH_3 and CH_2 stretching groups (Fig. 5B). The band at ~3014 cm^{-1} was mainly due to unsaturation in the acyl chain of phospholipids in the brain tissue (Akkas et al., 2007). DLM alone treated group showed significant ($P < 0.001$) decrease by 53.33% in the area of band at ~3014 cm^{-1} DLM alone treated group compared to control, whereas in TMR co-administrated with DLM (DLM + TMR) group shows restoration in the unsaturation in the acyl chain of phospholipids (Table 6). One more important band observed at ~2856 cm^{-1} is assigned to the saturated lipids in the brain tissue (Akkas et al., 2007). The band area of this was decreased significantly ($P < 0.001$) in the DLM alone treatment group compared to control. However, the ratio of saturated to unsaturated lipids was significantly increased in the DLM alone treated group compared to control (Table 6). TMR co-administration with DLM in DLM + TMR group showed appreciable restoration in the area and ratio value of unsaturated and saturated lipids in brain tissue (Tables 4 and 5). The bands at ~2962 cm^{-1} and ~2924 cm^{-1} were assigned to the methyl and methylene groups of lipids respectively in the brain tissue. The area values were significantly ($P < 0.001$) decreased from 0.16 ± 0.09 to 0.09 ± 0.01 in methyl and from 2.98 ± 0.11 to 1.47 ± 0.55 in the methylene population in the brain tissue of DLM alone treated group compared to control. The group feed with *turmeric-diet* with simultaneous DLM exposure in DLM + TMR group showed restoration in the values of these bands towards the control, while the group feed merely on *turmeric-diet* showed insignificant ($P > 0.05$) changes compared to control (Table 6).

Fig. 5C shows that absorptions are primarily due to the continuation of polysaccharides, nucleic acid, phospholipids and carbohydrates in the range of ~1800-800 cm^{-1}. The band assignments are given in Table 3. The main band at ~1240 cm^{-1} was due to the asymmetric phosphate stretching vibration of phospholipids and the band observed at ~1160 cm^{-1} was due to C–O asymmetric stretching of glycogen. Significant ($P < 0.001$) decrease in the area from 2.06 ± 0.05 to 1.39 ± 0.005 and 0.02 ± 0.00 to 0.01 ± 0.00 in phospholipids and glycogen respectively of these bands was observed in the DLM alone treatment group compared to control, whereas TMR co-administrated with DLM (DLM + TMR) group showed appreciable restoration the area values of these bands compared to DLM alone treated group, while the group fed merely on *turmeric-diet* showed insignificant ($P > 0.05$) changes compared to control (Table 6).

Fig. 6A shows the changes in the secondary structure of protein and the changes in the peak position, peak intensity and peak assessments are given in the Table 6. The intensity of all the bands were affected in the DLM alone treated group compared to control. The intensity of the antiparallel β-sheet and random coil structure was significantly increased in the DLM treated group compared to control. DLM alone treated group showed a significant decrease in the intensity of the α-helix, β-sheet and aggregated β-sheet significant increase in the antiparallel β-sheet and random coils compared to control. While the group co-administrated with TMR (DLM + TMR)

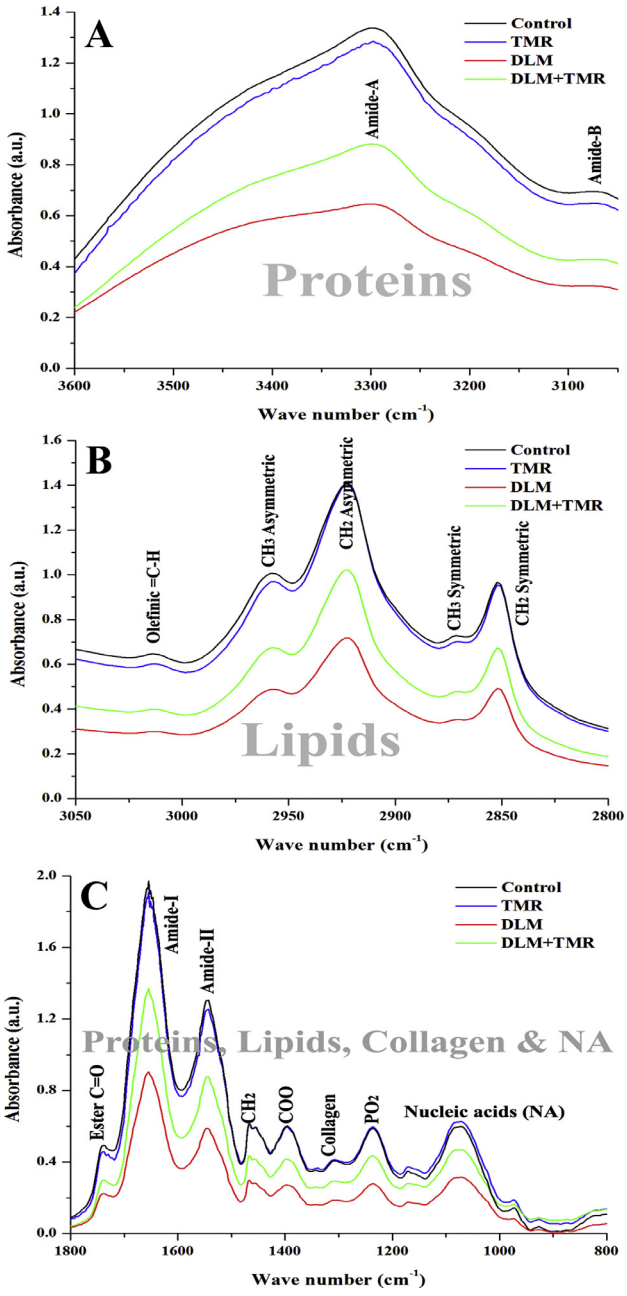

Fig. 5 The FT-IR spectra of rat brain tissues in the control., merely fed on *turmeric-diet* (TMR)., deltamethrin (DLM) treated and TMR co-administrated with DLM (DLM + TMR) groups in the ~3600–3050 cm^{-1} (A), ~3050–2800 cm^{-1} (B) and ~1800–800 cm^{-1} regions.

showed the restoration in the intensity of all peaks compared to DLM alone treated group.

Fig. 6B shows changes in the lipid containment of control and treated rat brain tissue in the region from ~3050 to 2800 cm^{-1}. The two bands are mainly due to CH_2 asymmetric and symmetric stretching in the brain tissue (Table 6). The intensities of the CH_2 asymmetric and symmetric stretching bands decreased significantly in the DLM-treated brain tissues, which correspond to decrease in the lipid content, while in the group co-administrated with TMR showed significant

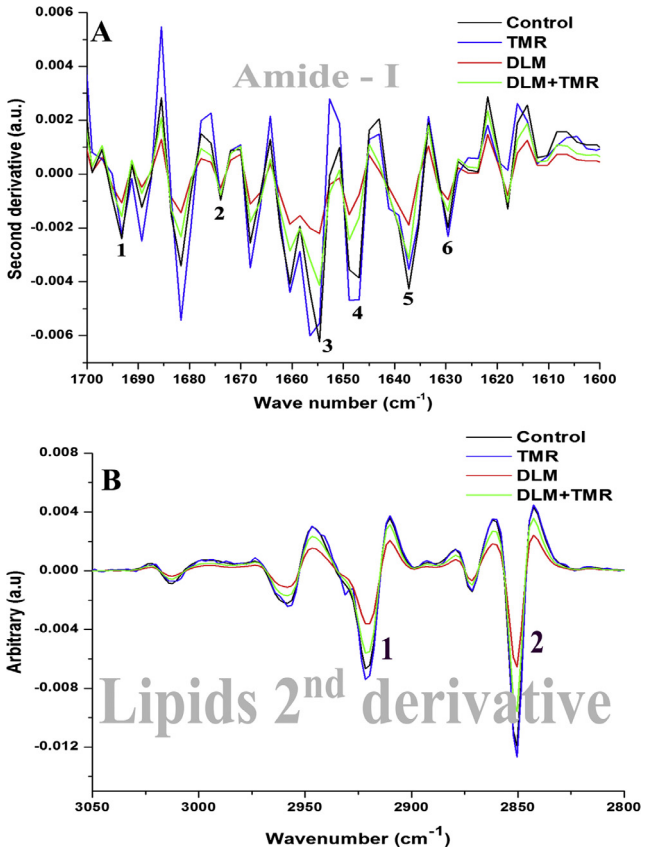

Fig. 6 Second derivative Fourier transform-infrared (FT-IR) spectra in the ~1700–1600 cm^{-1} (A) and ~3050–2800 cm^{-1} (B) region of the control., merely fed on *turmeric-diet* (TMR)., deltamethrin (DLM) treated and TMR co-administrated with DLM (DLM + TMR) groups rat brain tissues.

restoration in the brain contain compare to DLM alone treated group. The group merely feed with *turmeric-diet* (DLM + TMR) showed insignificant changes in the intensity compared to control.

Discussion

Usage of insecticides and pesticides has been increased, as there is a great demand for food production for increased population. Therefore, it is undeniable for the Government to give permission for the production of more number of pesticide or insecticides, however, preferably those are less mammalian and high insect toxic. Pyrethroids are the class of insecticides that cause low mammalian and high insect toxicity (Haverinen and Vornanen, 2014). Now a days increased use of pyrethroids cause a number of neurodegenerative diseases in humans (Baltazar et al., 2014). These diseases are mainly because of oxidative damage and imbalance in lipid metabolism in the neural tissue (Roszczenko et al., 2013). Fendri et al. (2009) demonstrated that neurons in the nervous system are more susceptible to free radical toxicity as they have a high amount of catecholamine oxidative metabolic activity and contain low levels of antioxidant enzymes. Studies reported that pyrethroids cause oxidative stress in neural tissue (Kim et al., 2006; Gullick et al., 2014). Together, it is predictable that oxidative damage is a key to the aetiology of neurodegenera-

Table 4 Changes in the band areas IR bands for the control, TMR, DLM alone treated and TMR co-administrated with DLM brain tissues of rats ($n = 6$).

Wave number (cm^{-1})	Experimental groups			
	Control	TMR	DLM	DLM + TMR
3301	255.81 ± 3.11	261.88 ± 2.13	181.36 ± 8.31***	223.39 ± 7.10^{+++}
3085	0.49 ± 0.01	0.52 ± 0.01	0.35 ± 0.02 ***	0.43 ± 0.01^{++}
3014	0.15 ± 0.01	0.14 ± 0.06	0.07 ± 0.005 ***	0.10 ± 0.007^{+}
2962	0.16 ± 0.09	0.15 ± 0.07	0.09 ± 0.01***	0.13 ± 0.03^{++}
2924	2.98 ± 0.11	3.00 ± 0.53	1.47 ± 0.55 ***	1.80 ± 0.58^{+}
2856	0.81 ± 0.03	0.76 ± 0.04	1.01 ± 0.04 ***	0.85 ± 0.03^{+}
1744	0.87 ± 0.01	0.83 ± 0.03	0.54 ± 0.04 ***	0.66 ± 0.05^{+}
1654	31.74 ± 0.71	36.69 ± 0.65	23.17 ± 0.78 ***	29.97 ± 0.51^{++}
1544	9.50 ± 0.32	10.84 ± 0.46	5.38 ± 0.24 ***	8.02 ± 0.28^{++}
1465	0.30 ± 0.09	0.34 ± 0.06	0.43 ± 0.02 ***	0.34 ± 0.09^{++}
1311	2.53 ± 0.08	2.67 ± 0.012	1.83 ± 0.04 ***	2.18 ± 0.05^{++}
1240	2.06 ± 0.05	2.14 ± 0.01	1.39 ± 0.05***	1.62 ± 0.03^{++}
1160	0.02 ± 0.00	0.02 ± 0.00	0.01 ± 0.00***	0.02 ± 0.00^{+}

Values are means ± SE for six rats in each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ for DLM and merely *turmeric-diet* fed (TMR) groups vs. control group and $^{+}P < 0.05$; $^{++}P < 0.01$: (DLM + TMR) group vs. DLM group.

Table 5 FT-IR absorption band area ratio for selected bands of control, TMR, DLM treated and TMR co-administrated with DLM treated brain tissues of rat.

Band area ratio	Experimental groups			
	Control	TMR	DLM	DLM + TMR
I_{1544}/I_{3301}	0.042 ± 0.002	0.043 ± 0.002	0.023 ± 0.001***	0.032 ± 0.001^{++}
I_{2962}/I_{2856}	0.19 ± 0.009	0.20 ± 0.005	0.09 ± 0.006***	0.16 ± 0.01^{++}
I_{1544}/I_{1654}	0.29 ± 0.006	0.29 ± 0.008	0.23 ± 0.009***	0.26 ± 0.10^{+}

Values are means ± SE for six rats in each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ for DLM and merely *turmeric-diet* fed (TMR) groups vs. control group and $^{+}P < 0.05$; $^{++}P < 0.01$: (DLM + TMR) group vs. DLM group.

Table 6 Band assignments of the secondary derivative and peak intensity of amide-I band (~1700–1600 cm^{-1}) and lipid band (~3050–2800 cm^{-1}) region of control, turmeric (TRM), deltamethrin (DLM) and TMR co–administered with DLM treated brain tissues based on the literature (Quitschke et al., 2013; Samini et al., 2013; Sethi et al., 2009; Sebnem et al., 2007; Shafer et al., 2005; Sharma, 1976).

Wave number in cm^{-1}					Peak intensity (au)				Peak assignments
Peak No	Control	TMR	DLM	DLM + TMR	Control	TMR	DLM	DLM + TRM	
Protein									
1	1693	1693	1693	1693	−0.0010	−0.0015	−0.0023**	−0.0022^{+}	Antiparallel β-sheet
2	1673	1673	1673	1673	−0.0009	−0.0009	−0.0005*	−0.0007^{+}	Turns
3	1654	1654	1654	1654	−0.0061	−0.0057	−0.0021***	−0.0041^{++}	α-helix
4	1646	1646	1648	1648	−0.0015	−0.0016	−0.0041***	−0.0038^{+}	Random coil
5	1637	1637	1637	1637	−0.0037	−0.0035	−0.0018**	−0.0031^{++}	β-sheet
6	1629	1629	1629	1629	−0.0019	−0.0021	−0.0009***	−0.0013^{++}	Aggregated β-sheet
Lipid									
1	2921	2921	2921	2921	−0.006	−0.007	−0.003**	−0.005^{+}	CH_2 asymmetric stretching
2	2850	2850	2850	2850	−0.011	−0.012	−0.006***	−0.009^{++}	CH_2 symmetric stretching

Values are means ± SE (±0.0003) for six rats in each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ for DLM and merely *turmeric-diet* fed (TMR) groups vs. control group and $^{+}P < 0.05$; $^{++}P < 0.01$: (DLM + TMR) group vs. DLM group.

tive disorders. Thus, it had drawn the attention of a number of researchers to find out capable antioxidants in order to reduce oxidative damage. Therefore, in the present study, we have made an attempt with turmeric for its efficient antioxidant capacity. Naksuriya et al. (2010) and Lim et al. (2001) have suggested that curcumin plays an important role in the neuroprotection and reduced amyloid pathology in Alzheimer transgenic mice. However, none of the studies dealt with the neuroprotection effect of turmeric as a whole, against pyrethroid induced neural toxicity. This study explores the ameliorative effect of turmeric against DLM caused oxidative stress leads to neurodegenerative diseases in the brain tissue of albino

rats at the molecular level using FT-IR spectroscopy and biochemical analysis. The FT-IR investigation provides structural information of biomolecules including proteins, nucleic acids, carbohydrates and lipids, and it allows for recognition, detection and quantification of changes in these macromolecular components (Sivakumar et al., 2014).

In the present study care has been taken while preparing *turmeric-diet* and preservation and also the preparation of uniform thickness of pellet with same quantity of sample and KBr (1:100) for FT-IR analysis. The spectra were collected in triplet and observed that they were identical. Therefore, it is possible to directly relate the change in intensity and more accurately the area of the absorption bands to the concentration of the corresponding biomolecules in the tissue (Akkas et al., 2007; Kong and Yu, 2007; Cakmak et al., 2006).

Fig. 5A and Table 3 show shifting in the frequency of amide-A and amide-B band at ~3301 cm^{-1} and ~3078 cm^{-1} respectively, which are mainly due to N–H stretching of proteins with a negligible contribution from O–H stretching of intermolecular hydrogen bonding since unbound water was removed from the system (Cakmak et al., 2006). The shift towards lower values and significant decreases ($P < 0.01$) in the area of these bands were observed in the DLM alone treated rats (Tables 3 and 4). The decrease in the area value of these bands indicates, that there is decrease in protein content in the brain tissue (Akkas et al., 2007; Sivakumar et al., 2014), while in the TMR co-administrated with DLM (DLM + TMR) group was showed significant ($P < 0.05$) restoration in these band areas. The increase in the area of amide-A and amide-B bands indicates an increase in the protein synthesis in the brain tissue. This is the supportive sign of the ameliorative effect of turmeric over the pyrethroids induced oxidative stress or neurodegenerative diseases in the brain. These findings agree with the findings of Quitschke et al. (2013), who demonstrated that, the curcumin exhibits protective effect against Alzheimer disease. The group merely fed with *turmeric-diet* (TMR) showed insignificant ($P > 0.05$) changes in the area values and the area ratio of these bands (Tables 3 and 4).

Several other studies demonstrated that the brain is a lipid-rich tissue having relatively low antioxidative potential, is especially susceptible to the action of xenobiotic compounds, those can induce oxidative stress and disturbing lipid metabolism (Ong et al., 2010). Roszczenko et al. (2013) demonstrated that nervous tissue contains a higher level of peroxidizable unsaturated lipids and high oxygen utilization and more susceptible to peroxidative damage than other organs. As seen from the Fig. 5B and Table 6, the area of the olefinic band decreased significantly ($P < 0.001$) in the DLM alone treated group, indicating decreased 53.33% in the population of unsaturation in acyl chains of lipid molecules. This band was used as an index of relative concentration of the unsaturated lipids. Ozek et al. (2010) have demonstrated that the decrease in the unsaturation is responsible for the increased lipid peroxidation caused by ROS. This was observed by the secondary derivative of the lipid band in the ~3050–2800 cm^{-1} region (Fig. 6B). TMR co-administration with DLM in (DLM + TMR) group shows a significant increase in the band area of olefinic unsaturated fatty acids. Such increases in the area of olefinic band reveal that TMR can reduce the free radical damage in the lipid molecules in the brain tissue of rats. Studies demonstrated that the turmeric polyphenolic compounds can scavenge the free radical generated in the functionally different tissues (Fu et al., 2014; Yang et al., 2014). It implies that damage caused by ROS in brain tissue may be reduced by turmeric supplemented diet offered to DLM + TMR group rats. The band observed at ~3014 cm^{-1} gives information about the concentration of unsaturated lipid, olefinic HC–CH stretching band and observed band at ~2856 cm^{-1} about saturated lipids, CH_2 symmetric. This result indicates that DLM caused a significant ($P < 0.01$) increase in the ratio of saturated lipids to unsaturated lipids (Table 6). With this ratio it has been confirmed that DLM causes degradation of lipid in the brain tissue. The decrease in intensity of band at ~1744 cm^{-1} also provides the proof of decreased quantity of unsaturated acyl chain in the DLM treated rats (Sebnem et al., 2007). Several studies reported that DLM causes lipid peroxidation by generating ROS that further cause lipid degradation. However, lipid integrities are playing an important role in regulating many membrane functions, such as signal transduction, solute transport, and activity of enzymes associated with the membrane. Lipid peroxidation causes the decrease of CH_2 bonds in lipid chains and the production of lipid hydroperoxides, which react with other lipids giving rise to an auto-oxidation cycle that damage deeply cellular membrane (Ozek et al., 2010). The studies provide evidence that changes in the membrane fluidity and order of the lipid affect the kinetics and function of different ionic channels, including sodium, potassium, and chloride, and thus alters the membrane excitability (Awayda et al., 2004; Sirvent et al., 2008). Probably such change in lipid order and dynamics plays the main role in prolonged opening of ion channels which, further may cause trailing current in the signalling, therefore, neurodegenerative diseases in the brain. The biomedical analysis in the brain tissue was helped to confirm the same. All these observations in merely feed *turmeric-diet* (TMR) group were same as in the control.

Biochemical estimation revealed that the DLM treatment induced significant ($P < 0.001$) increase in the MDA level by 42.05% (Fig. 2). On the other hand DLM alone treatment significantly reduces the activity of SOD, CAT, GPx and GR in the brain tissue (Table 2). These findings coincide with the findings of Fetoui et al. (2008). TMR co-administration with DLM showed restoration in the MDA level and in all antioxidant enzyme activity. Studies show that curcumin can distribute throughout the body, including the brain and it can inhibit or scavenge the ROS generated in the cells and tissue (Sharma, 1976; Nishikawa et al., 2013; Quitschke et al., 2013). Curcumin is shown to be neuroprotective, against ethanol and aluminium induced brain damage (Sethi et al., 2009; Quitschke et al., 2013) and most importantly, it reduces amyloid pathology in Alzheimer transgenic mice (Lim et al., 2001).

DLM can alter the cellular reduced glutathione level, resulting in excessive production of ROS at the mitochondrial level, leading to damage of cellular components. GSH plays an important role in the balancing the generated ROS in cells. On the other hand, decreased level of GSH may lead to the increased lipid peroxidation in the brain tissue. In the present study, the GSH content was significantly ($P < 0.001$) decreased in the DLM treated group (Fig. 3). Studies demonstrated that pyrethroids can cause oxidative stress by decreasing the level of GSH in functionally different tissues (Sirvent et al., 2008; Fendri et al., 2006; Rajakrishnan et al., 1999). Reduced GSH level leads to accumulating H_2O_2 and promote the formation of OH^-, the most toxic molecule, it results in more oxidant load and so oxidative damage (Ishrat et al.,

2009). However, the brain is rich in polyunsaturated fatty acids, highly susceptible to the free radicals (Gilda et al., 2010). Enhanced ROS and decreased activity of antioxidants result in the conversion of polyunsaturated fatty acids to saturated fatty acids in the brain tissue. Altogether, we conclude that pyrethroids induce oxidative damage in the neural tissue results into neurodegenerative diseases in human and animals. TMR co-administration with DLM (DLM + TMR) group is significant ($P < 0.05$) in restoration of the activity of antioxidants (Table 2). The ratio calculation show increased saturated fatty acids over unsaturated fatty acids in DLM treated group (Table 6). While in the TMR co-administered group observed restoration in these biomolecules, which indicates that the turmeric is one of the good neuroprotector. The group feed merely with *turmeric-diet* (TMR) shows insignificant ($P > 0.05$) changes in saturated and unsaturated fatty acid ratio. Studies demonstrated that turmeric contain phenolic compounds like curcumin, it acts as anti-epileptic agent by scavenging ROS (Fendri et al., 2006). The antioxidant activity of phenolics is mainly due to their redox properties, which allow them to act as reducing agents, hydrogen donators and singlet oxygen quenchers (Kähkönen et al., 1999; Kaur and Kapoor, 2002). Consequently, the present study shows that turmeric supplemented diet acts as good antagonistic compound against neurodegenerative diseases caused by DLM.

Fig. 5C and Table 5 show the changes in the ratio of methyl and methylene band at ~2962 cm^{-1} and ~2856 cm^{-1} respectively. DLM alone treatment was significantly brings down the ratio of methyl group protein. This may be due to generated ROS can cause structural modification in proteins via conversion of side chain amino groups to the corresponding free radical-induced carbonyls (C═O) at arginine, lysine, threonine or proline residues (Aksenov et al., 2001). While the TMR co-administration with DLM restore the methyl ratio in DLM + TMR group. The bands from ~1700–1600 cm^{-1} are assigned to α-helix structure and β-sheet structures of proteins (Toyran et al., 2004). Fig. 5B and Table 3 shows the changes in the frequency and the area value of amide-I and amide-II at ~1654 cm^{-1} and ~1544 cm^{-1} respectively. However, it is seen in Table 4 the area values of these bands were significantly decreased in the DLM alone treated group. The decrease in the band area of amide-I and amide-II was consistent with the decrease in band area of amide-A band at ~3301 cm^{-1}. These, bands of the proteins are mainly responsible for the other action in secondary structure of proteins. Significant ($P < 0.001$) reduction in the area values of these bands indicates that there is a decrease in the membrane proteins, including, α- and β-proteins of the ion channels in the neurons. The maxima of amide-I region (~1700–1600 cm^{-1}) is used for the protein secondary structure analysis (Surewicz and Mantsch, 1988). The decreased in the intensity of α-helix, β-sheets and turns which is accompanied by increase in the intensity of antiparallel β-sheets and random coils in the proteins has been observed in the DLM treated rat brain tissue (Fig. 6A, Table 6). Aksenov et al. (2001) demonstrated that the pyrethroids cause decrease in the protein content of the brain. The loss of the protein, mainly takes place by the breakdown of the hydrogen and sulphide bands in the proteins. Such breaks can lead to the unfolding of the proteins and results in a disorganization of the internal structure (Toyran et al., 2005). The secondary structure analysis indicates that the DLM mainly cause the unfolding of the α-helix and β-sheet by increasing the antiparallel β-sheet and random coils (Table 6). Due to conformal changes in these protein secondary structure, channels may remain open which leads to slow neural transduction. All these changes are mainly due to oxidative damage in the neural tissue caused by ROS. However, TMR co-administration with DLM shows restoring the structural changes in these proteins. Which is confirmed by shift in the band frequency DLM + TMR group. The group merely fed with *turmeric-diet* (TMR) showed insignificant ($P > 0.05$) changes in protein content. The increased ratio of amide-II to amide-I confirm that turmeric restores the protein structure in brain tissue (Table 6). The secondary structure of the protein was restored by decreasing the antiparallel β-sheets and random coils and increasing the α-helix and β-sheet in the TMR co-administered rat brain (Table 4). Similar to these changes in the amide-I and amide-II, also confirmed by biochemical improvement in the activity of antioxidant enzymes and revels the oxidative damage to the proteins. Wang et al. (2013) had reported that curcumin cross the blood–brain barrier and inhibit the formation of amyloid β-oligomers and fibrils in mice, so it has been recommended that the use of curcumin for the clinical trials to prevent or to treat Alzheimer's disease. The curcumin treatment decreases the oxidization of the proteins in the brain tissue (Ataie et al., 2010). Additionally, several other studies were reported that curcumin is one of the preeminent protectors against Alzheimer's disease (Samini et al., 2013; Yang et al., 2005).

In conclusion, we have showed that DLM causes oxidative damage by decreasing the activity of antioxidants in the rat brain tissue. 1% *Turmeric-diet* was ameliorated against oxidative stress in the neural tissues in animals and human. However, the protective effect of turmeric was successfully evidenced by FT-IR analysis, including restoration of the unsaturated fatty acids, protein contain and in the activity of antioxidants. The present findings add to the current knowledge on the usage of protective use of turmeric to prevent the oxidative damages in the neural tissue caused by DLM.

Conflict of interest

The authors declare that there are no conflicts of interest.

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Further reading

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