ISSN : 2350-0743

www.ijramr.com

International Journal of Recent Advances in Multidisciplinary Research
Vol. 02, Issue 12, pp.5753-5753, December, 2015

RESEARCH ARTICLE

A REVIEW ON CURCUMIN COMPARE TETRAHRDOCURCUMIN ON DIABETES

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ARTICLE INFO

Article History:
Received 26th, September 2015
Received in revised form
06th, October 2015
Accepted 30th, November 2015
Published online 30th, December 2015

Keywords:
Antioxidants, Tetrahydrocurcumin, Curcumin, Lipid Peroxidation. Glucose, Insulin

ABSTRACT

Turmeric, a spice that has long been recognized for its medicinal properties, has received interest from both the medical/scientific world and from culinary enthusiasts, as it is the major source of the polyphenol curcumin. The use of turmeric, derived from the root of the plant *Curcuma longa*, for treatment of different inflammatory diseases has been described in Ayurveda and in traditional Chinese medicine for thousands of years. The active component of turmeric responsible for this activity, curcumin, was identified almost two centuries ago. Anti-viral, Anti-oxidant, Anticancer, Anti-bacterial, Anti-asthmatic, Antiarthritis, Anti-diabetic, Anti-venom, Antiobesity, Wound-healing, in depression and anxiety and other activities. Various clinical trials and their observations regarding these activities have been discussed here. Curcumin is a tautomeric compound existing in enolic form in organic solvents and as a keto form in water. This review article summarizes a various role and activity of Curcumin. Tetrahydrocurcumin (THC) is one of the major colourless metabolite of curcumin. THC has been reported to exhibit the same physiological and pharmacological properties of curcumin.

INTRODUCTION

The turmeric (Curcuma longa) plant, a perennial herb belonging to the ginger family, is cultivated extensively in south and southeast tropical Asia. The rhizome of this plant is also referred to as the "root" and is the most useful part of the plant for culinary and medicinal purposes. The most active component of turmeric is curcumin, which makes up 2–5% of the spice. The characteristic yellow color of turmeric is due to the curcuminoids, first isolated by Vogel in 1842. Curcumin is an orange-yellow crystalline powder practically insoluble in water. The structure of curcumin (C21H20O6) was first described in 1910 by Lampe and Milobedeska and shown to be diferuloylmethane. Turmeric is used as a dietary spice, coloring agent in foods and textiles, and a treatment for a wide variety of ailments. It is widely used in traditional Indian medicine to cure biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis. Turmeric paste in slaked lime is a popular home remedy Turmeric is used as a dietary spice, coloring agent in foods and textiles, and a treatment for a wide variety of ailments. It is widely used in traditional Indian medicine to cure biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis. Turmeric paste in slaked lime is a popular home remedy for the treatment of inflammation and wounds. For centuries, curcumin has been consumed as a dietary spice at doses up to 100 mg/day.

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Recent phase I clinical trials indicate that human beings can tolerate a dose as high as 8 g/day with no side effects. The focus of this review is to describe the effect of curcumin in various diseases. *Curcuma longa* is commonly used in the treatment of diabetes by ayurvedic physicians. Curcumin is a biologically active component isolated from the rhizome of Curcuma longa that possess antihyperglycemic activity (Arun and Nalini, 2002), hypolipidemic action (Suresh Babu and Srinivasan, 1997) and anti - renal lesion effect (Suresh Babu and Srinivasan, 1998). The use of curcumin is recommended for prevention of advanced glycated endproducts (AGE) accumulation and the associated complications of diabetes (Sajithlal et al., 1998).

Tetrahydrocurcumin (THC) is one of the major colourless metabolite of curcumin. THC has been reported to exhibit the same physiological and pharmacological properties of curcumin (Majeed et al., 1995 and Sugiyama et al., 1996). Curcumin is rapidly metabolized during absorption from the intestine, yielding THC (Ravindranath and Chandrasekara, 1980), which has shown the strongest antioxidant activity among all curcuminoids (Osawa et al., 1995). Several studies in experimental animals indicated that THC also prevent(s) cancer (Lin and Lin-Shiau, 2001), protect(s) against inflammation (Nakamura, 1998 and Hong et al., 2004), atherosclerotic lesions (Naito et al., 2002) and hepatotoxicity (Pari and Murugan, 2004). In our previous study, we have demonstrated the antidiabetic effect of THC in streptozotocin (STZ) induced diabetic rats (Pari and Murugan, 2005, Murugan and Pari, 2006; Murugan and Pari, 2007).

RESULTS

Figure 1 and 2 shows the level of blood glucose, total haemoglobin, glycosylated haemoglobin and plasma insulin of different experimental groups.

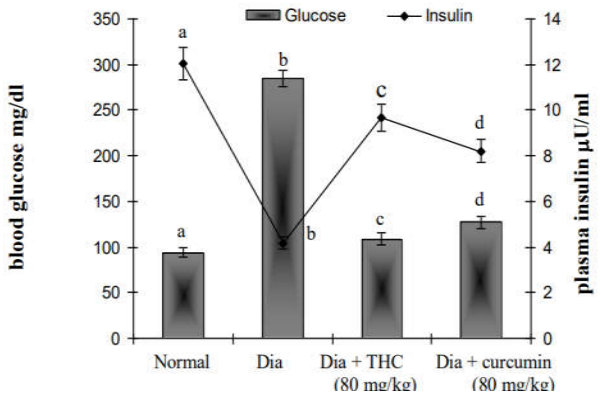

Figure 1. Effect of tetrahydrocurcumin (THC) on the levels of blood glucose and plasma insulin in normal and experimental rats. Dia - Diabetic control. Values are given as mean ± S.D for 6 rats in each group. Values not sharing a common superscript letter differ significantly at p<0.05(DMRT).

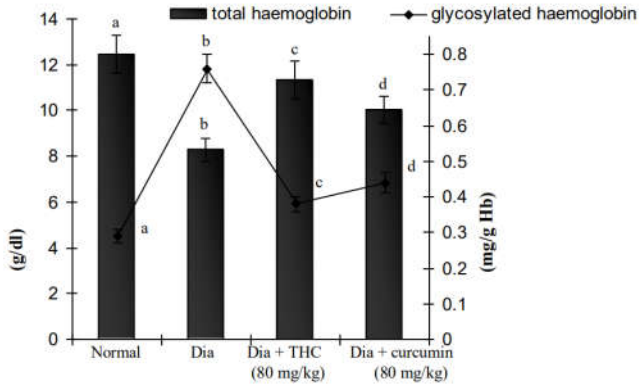

Figure 2. Effect of tetrahydrocurcumin (THC) on the levels of haemoglobin and glycosylated haemoglobin in normal and experimental rats. Values are given as mean ± S.D for 6 rats in each group. Values not sharing a common superscript letter differ significantly at p<0.05(DMRT).

There was a significant elevation in blood glucose level, whereas plasma insulin levels decreased significantly in diabetic rats, compared with normal rats. Administration of THC and curcumin tended to bring blood glucose and plasma insulin towards normal. The diabetic control rats showed a significant decrease in the level of total haemoglobin and significant increase in the level of glycosylated haemoglobin. Oral administration of THC and curcumin to diabetic rats significantly restored total haemoglobin and glycosylated haemoglobin levels. The effect of THC was more prominent when compared with curcumin. Table 1 represents the effect of THC on glycogen content in liver and muscle of normal and experimental animals. In diabetic controls, hepatic and skeletal muscle glycogen content was decreased significantly as compared to non-diabetic controls. Treatment with THC and Curcumin significantly increased the hepatic and skeletal glycogen. Table 2 depicts the activities of carbohydrate metabolizing enzymes in liver of normal and THC treated diabetic rats. The activities of enzyme hexokinase and glucose-6-phosphate dehydrogenase was found to be decreased whereas the activities of sorbitol dehydrogenase and gluconeogenic enzymes: glucose-6-phosphatase, fructose-1,6-bisphosphatase and sorbitol dehydrogenase were significantly increased in diabetic control rats. THC administration to diabetic rats significantly reversed the above changes when compared to diabetic control rats. The levels of serum and tissues cholesterol, free fatty acids, triglycerides and phospholipids of normal and experimental rats are given in table 3. Cholesterol, free fatty acids, triglycerides and phospholipids were significantly decreased in THC and curcumin treated rats as compared to diabetic rats. Oral administration of THC at (80 mg/kg) and curcumin (80 mg/kg) significantly decreased the levels of serum and tissue lipids as compared to untreated diabetic rats. The THC administration showed more effective than curcumin. Table 4 represents the concentration of TBARS and hydroperoxides in tissues of normal and experimental rats. There was a significant elevation in tissue TBARS and hydroperoxides during diabetes, when compared to the corresponding normal group. Administration of THC and curcumin significantly decreased the lipid peroxidation in diabetic rats. The effect of THC was more potent than curcumin. For studying the effect of THC on free radical production, the activities of SOD, CAT, GPx, GST, GSH, vitamin C and vitamin E were measured (table 5 and 6). They presented significant increases in THC treatment when compared with diabetic control rats. The effect of THC was more prominent compared with curcumin.

DISCUSSION

Diabetes mellitus is spreading in an alarming way throughout the world and three fourth of the world populations and considered as a major cause of high economic loss which can in turn impede the development of nations. Moreover, uncontrolled diabetes leads to many chronic complications such as blindness, heart disease, and renal failure, etc. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Therefore, treating diabetes mellitus with plant derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive. THC to decrease the elevated blood sugar level to normal glycemic level is an essential trigger for the liver to revert to its normal homeostasis during experimental diabetes. The possible mechanism by which THC bring about its antihyperglycemic action in diabetic rats may be by increasing the pancreatic secretion of insulin from the existing β– cells or insulin release from bound form which was evidenced by the significant increase in the level of insulin in THC treated diabetic rats. Administration of THC to normal rats showed a significant decrease in the level of blood glucose and increase in the level of plasma insulin (Table 1). This clearly shows that the THC has better effect on secretion of insulin from pancreatic β - cells. It is well documented that the body weight was decreased in diabetic rats (Al-Shamaony, 1994). Administration of THC to diabetic rats significantly reversed the loss in body weight and that seems to be to its ability to reduce hyperglycemia (Table 1). In uncontrolled or poorly controlled diabetes, there is an increased glycation of a number of proteins including haemoglobin and alpha- crystalline of lens. Glycosylated haemoglobin was significantly increased in diabetic control animals, and this increase is directly proportional to fasting blood glucose \38\.

Table 1. Effect of THC on the levels of liver and muscle glycogen in normal and experimental rats

Groups	Glycogen (mg/g tissue)	
	Liver	*Muscle*
Normal	33.25 ± 1.65^{a}	6.63 ± 0.25^{a}
Diabetic control	20.54 ± 1.56^{b}	3.66 ± 0.17^{b}
Diabetic + THC (80 mg/kg)	29.35 ± 1.58^{c}	5.85 ± 0.21^{c}
Diabetic + Curcumin (80 mg/kg)	26.73 ± 1.44^{d}	5.48 ± 0.15^{d}

Values are given as mean ± SD from 6 rats in each group.
Values not sharing a common superscript letter differ significantly at $p<0.05$ (DMRT).

Table 2. Effect of THC on the activities of hepatic hexokinase, glucose-6-phosphate dehydrogenase, glucose-6-phosphatase, fructose-1, 6-bisphosphatase and sorbitol dehydrogenase in normal and experimental rats

Groups	Normal	Diabetic control	Diabetic + THC (80 mg/kg)	*Diabetic + Curcumin (80mg/kg)*
Hexokinase (units[1]/g protein)	148.62 ± 8.27^{a}	109.37 ± 6.46^{b}	138.11 ± 5.61^{c}	124.72 ± 6.98^{d}
Glucose-6-phosphate dehydrogenase (x 10^{-4} mIU / mg protein)	4.61 ± 0.14^{a}	2.16 ± 0.11^{b}	3.74 ± 0.18^{c}	3.35 ± 0.10^{d}
Glucose- 6-phosphatase (units[2]/ mg protein)	0.16 ± 0.01^{a}	0.25 ± 0.02^{b}	0.18 ± 0.01^{c}	0.20 ± 0.01^{d}
Fructose-1,6-bisphosphatase (units[3]/ mg protein)	0.35 ± 0.03^{a}	0.55 ± 0.03^{b}	0.40 ± 0.02^{c}	0.45 ± 0.03^{d}
Sorbitol dehydrogenase (units[4]/ g protein)	4.28 ± 0.33^{a}	8.47 ± 0.64^{b}	5.64 ± 0.43^{c}	6.24 ± 0.47^{d}

Values are given as mean ± SD from 6 rats in each group.
Values not sharing a common superscript letter differ significantly at $p<0.05$ (DMRT).
1 - µmoles of glucose phosphorylated/min
2 - µmoles of Pi liberated/min
3 - µmoles of Pi liberated/hour
4 - 1 unit of sorbitol dehydrogenase = the amount of enzyme that produces a change in absorbance of 0.01/min

Table 3. Effect of THC on the levels of cholesterol, free fatty acids, triglycerides and phospholipids in serum, liver and kidney of normal and experimental rats

Groups	Normal	Diabetic control	Diabetic + THC (80 mg/kg)	Diabetic + Curcumin (80 mg/kg)
	Cholesterol			
Serum (mg/100ml)	88.78 ± 5.27^{a}	170.02 ± 11.67^{b}	110.94 ± 7.05^{c}	129.02 ± 7.03^{d}
Liver (mg/100g wet tissue)	328.88 ± 19.54^{a}	517.08 ± 35.51^{b}	417.52 ± 26.54^{c}	447.67 ± 30.74^{c}
Kidney(mg/100g wet tissue)	383.36 ± 22.77^{a}	541.23 ± 37.16^{b}	427.07 ± 23.27^{c}	457.86 ± 29.11^{c}
	Free fatty acids			
Serum (mg/100ml)	79.19 ± 4.70^{a}	147.88 ± 10.15^{b}	91.77 ± 5.83^{c}	107.02 ± 5.83^{d}
Liver (mg/100g wet tissue)	610.35 ± 36.26^{a}	860.13 ± 59.06^{b}	745.28 ± 47.38^{c}	794.13 ± 43.27^{c}
Kidney(mg/100gwet tissue)	433.80 ± 25.77^{a}	692.13 ± 47.53^{b}	544.59 ± 34.62^{c}	592.09 ± 32.26^{d}
	Triglycerides			
Serum (mg/100ml)	56.49 ± 3.36^{a}	95.57 ± 6.56^{b}	64.54 ± 4.10^{c}	77.01 ± 4.19^{d}
Liver (mg/100g wet tissue)	344.01 ± 20.44^{a}	628.75 ± 43.17^{b}	427.60 ± 27.18^{c}	529.08 ± 28.83^{d}
Kidney(mg/100gwet tissue)	272.38 ± 16.18^{a}	456.32 ± 20.27^{b}	377.18 ± 23.98^{c}	424.66 ± 16.07^{d}
	Phospholipids			
Serum (mg/100ml)	112.99 ± 6.71^{a}	175.04 ± 12.02^{b}	130.10 ± 8.27^{c}	152.54 ± 8.79^{d}
Liver (g/100g wet tissue)	1.66 ± 0.11^{a}	3.13 ± 0.19^{b}	1.99 ± 0.15^{c}	2.20 ± 0.13^{d}
Kidney (g/100g wet tissue)	1.56 ± 0.11^{a}	2.31 ± 0.14^{b}	1.73 ± 0.12^{c}	1.96 ± 0.13^{d}

Values are given as mean ± S.D for 6 rats in each group.
Values not sharing a common superscript letter differ significantly at $p<0.05$ (DMRT).

Table 4. Influence of THC and curcumin on the content of TBARS and hydroperoxides in rats liver and kidney.

Groups	Normal	Diabetic control	Diabetic + THC (80 mg/kg)	Diabetic + Curcumin (80 mg/kg)
TBARS				
Liver (mM/100g tissue)	0.75 ± 0.05^{a}	1.85 ± 0.11^{b}	1.06 ± 0.07^{c}	1.35 ± 0.08^{d}
Kidney (mM/100g tissue)	1.76 ± 0.12^{a}	3.73 ± 0.22^{b}	1.98 ± 0.14^{c}	2.30 ± 0.13^{d}
Hydroperoxides				
Liver (mM/100g tissue)	80.15 ± 5.45^{a}	100.55 ± 5.93^{b}	87.09 ± 4.74^{ac}	93.86 ± 4.17^{c}
Kidney (mM/100g tissue)	55.85 ± 3.80^{a}	78.66 ± 4.64^{b}	61.39 ± 4.48^{c}	68.14 ± 3.87^{d}

Values are given as mean □ S.D for 6 rats in each group.
Values not sharing a common superscript letter differ significantly at $p<0.05$ (Duncan's Multiple Range Test).

Table 5. Influence of THC and curcumin on the CAT, SOD, GPx, and GST activities in rats liver and kidney

Groups	Normal	Diabetic control	Diabetic+THC (80mg/kg)	Diabetic+Curcumin (80mg/kg)
CAT (units/mg of protein)				
Liver	74.15 ± 4.41^{a}	47.79 ± 3.282^{b}	67.57 ± 4.30^{c}	58.01 ± 3.16^{d}
Kidney	35.21 ± 2.09^{a}	17.30 ± 1.19^{b}	28.24 ± 1.19^{c}	23.01 ± 1.25^{d}
SOD (units/mg of protein)				
Liver	6.56 ± 0.39^{a}	3.52 ± 0.24^{b}	5.75 ± 0.37^{c}	4.98 ± 0.27^{d}
Kidney	14.83 ± 0.88^{a}	9.96 ± 0.68^{b}	13.82 ± 0.88^{c}	12.70 ± 0.69^{d}
GPx (units/mg of protein)				
Liver	6.36 ± 0.38^{a}	3.22 ± 0.22^{b}	5.65 ± 0.36^{c}	4.20 ± 0.23^{d}
Kidney	4.44 ± 0.26^{a}	2.31 ± 0.16^{b}	4.34 ± 0.28^{a}	3.60 ± 0.19^{c}
GST (units/mg of protein)				
Liver	6.46 ± 0.38^{a}	3.62 ± 0.25^{b}	5.75 ± 0.37^{c}	5.45 ± 0.24^{d}
Kidney	5.15 ± 0.31^{a}	2.14 ± 0.15^{b}	4.78 ± 0.30^{c}	3.67 ± 0.20^{d}

Data are mean ± SD values for six rats in each group. Units are as follows: CAT, μM of H_2O_2 consumed per minute; SOD, 1 unit of activity equals the enzyme reaction that gave 50% inhibition of nitro blue tetrazolium reduction in 1 minute; GSH, micrograms of GSH consumed per minute; GST, mμ of 1-chloro-2, 4-dinitrobenzene-glutathione (CDNB–GSH) conjugate formed per minute. Values not sharing a common superscript letter differ significantly at $P < .05$ (Duncan's Multiple Range Test).

Table 6. Influence of THC and curcumin on content of vitamin C, vitamin E, and GSH in rats liver and kidney

Groups	Normal	Diabetic control	Diabetic +THC (80mg/kg)	Diabetic + Curcumin (80mg/kg)
Vitamin C (μM/mg of tissue)				
Liver	1.45 ± 0.03^{a}	0.91 ± 0.02^{b}	1.33 ± 0.04^{c}	1.14 ± 0.02^{d}
Kidney	1.06 ± 0.04^{a}	0.34 ± 0.02^{b}	0.89 ± 0.03^{c}	0.74 ± 0.02^{d}
Vitamin E (μM/mg of tissue)				
Liver	0.68 ± 0.03^{a}	0.13 ± 0.01^{b}	0.56 ± 0.02^{c}	0.45 ± 0.02^{d}
Kidney	0.47 ± 0.03^{a}	0.09 ± 0.01^{b}	0.39 ± 0.03^{c}	0.31 ± 0.02^{d}
GSH (mg/100 g of tissue)				
Liver	46.10 ± 2.74^{a}	23.84 ± 1.63^{b}	40.54 ± 2.58^{c}	32.80 ± 1.78^{d}
Kidney	35.11 ± 2.08^{a}	19.61 ± 1.35^{b}	30.05 ± 1.91^{c}	23.20 ± 1.27^{d}

Data are mean ± SD values for six rats in each group. Values not sharing a common superscript letter differ significantly at $P < .05$ (Duncan's Multiple Range Test).

Anemia is much more common disease in Type 2 diabetic patients, contributing to the pathogenesis of diabetic complications. In the present study, the decreased concentration of haemoglobin indicates the anemia in STZ diabetic rats, in as much as during diabetes, the excess glucose transport in the blood reacts with haemoglobin to form glycosylated haemoglobin. In the present study, hepatic and skeletal muscle glycogen content was reduced significantly in diabetic controls. Administration of THC prevented the depletion of glycogen content but could not normalize it. This prevention is due to stimulation of insulin release from β–cells of THC. The activity of hexokinase decreased significantly in the liver of diabetic rats \39\. Administration of THC of diabetic rats resulted in a significant reversal in the activity of hepatic hexokinase (Table 2). The increased activity of hepatic hexokinase causes the increase in glycolysis and utilization of glucose for energy production. Administration of THC have been observed to decrease the concentration of blood glucose in STZ diabetic rats which may be due to the increased level of insulin, since the administration of THC to diabetic rats showed a significant increase in the level of plasma insulin. The decrease in the concentration of blood glucose in diabetic rats given THC may also be as a result of increased liver hexokinase activity there by increased glycolysis. The activity of glucose-6-phosphate dehydrogenase decreased in the present diabetic rats, which may result in the diminished functioning of HMP shunt and thereby the production of reducing equivalent such as NADH and NADPH \40- 41\. In our study, administration of THC considerably increased the activity of glucose- 6-phosphate dehydrogenase. In the present study, an increase in the activity of sorbitol dehydrogenase in the liver of diabetic control rats was observed. Increased activity of sorbitol dehydrogenase in diabetic rats has been reported by Arun and Nalini (2002). As the concentration of glucose in the liver goes up in diabetic rats, more glucose is converted to sorbitol. The observed elevation in the activity of sorbitol dehydrogenase in diabetic rats may have been due to the increased availability of sorbitol. Sorbitol dehydrogenase activity was found to be significantly reduced on treatment with THC. The effect produced by THC may be due to decrease in blood glucose by increased activity of plasma insulin, which may prevent glucose to sorbitol conversion. The abnormal high concentration of serum lipids in diabetes is mainly due to the increase in the mobilization of free fatty acids from the peripheral depots, since the insulin inhibits the hormone sensitive lipase. On the other hand, glucagons, catecholamines and other hormones enhance lipolysis. The marked hyperlipemia that characterizes the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots (Al-Shamaony et al. 1994). Diabetic rats treated with THC and curcumin shown significant decrease in serum and tissue lipids, THC produced a better effect than the curcumin. The level of serum lipids usually increased in diabetes and such elevation represented as a risk factor for coronary heart disease (Al-Shamaony et al. 1994). The abnormal high concentration of serum lipids in diabetes is mainly due to the increase in the mobilization of free fatty acids from the peripheral depots,

since insulin inhibits the hormone sensitive lipase. In present study, we have observed higher levels of cholesterol, triglycerides, phospholipids and free fatty acids in liver and kidney of streptozotocin diabetic rats. Cholesterol is a powerful risk factor for many coronary heart diseases. The degree of hypercholesterolemia is directly proportional to the severity of diabetes (Zavaroni et al. 1989). The increase in liver cholesterol level in diabetic rats, which was observed in our study could be due to increased cholesterogenesis. The increased level of cholesterol in liver and kidney is due to the decreased level of HDL – cholesterol. This in turn results in decreased removal of cholesterol from extra-hepatic tissues by the HDL–cholesterol (Prince et al. 1999). Hypertriglyceridemia is one of the risk factors in coronary artery disease and diabetes mellitus is always associated with raised triglycerides. The increased level of triglycerides in streptozotocin diabetes observed in our study may be due to lack of insulin, which normally activates the enzyme lipoprotein lipase. Phospholipids are vital components of biomembranes and cholesterol is responsible for the increased synthesis of ischemic phospholipids (Marsch et al. 1976). In this context, higher levels of cholesterol, triglycerides and phospholipids have been observed in diabetic liver and kidney (Pari and Venkateswaran 2003). Oral administration of THC to diabetic rats reversed all the above changes.

The increased concentration of free fatty acids was observed in liver and kidney of diabetic rats. Elevated levels of free fatty acids may promote synthesis of phospholipids and cholesteryl esters by the liver (Frayn 1993). The observed rise in free fatty acid in the liver may be attributed to the increased transport of fatty acid as a result of excessive mobilization of fatty acids (Woodside 1972). The diabetic complication associated with renal tissue may be partly due to abnormality in lipid metabolism. Administration of THC decreased the free fatty acid in tissues such as liver and kidney. Increased lipid peroxidation under diabetic conditions can be due to increased oxidative stress in the cell as a result of depletion of antioxidant scavenger systems. Associated with the changes in lipid peroxidation the diabetic tissues showed decreased activities of key antioxidants SOD, CAT, GSH, GPx, GST, GSH, vitamin C and vitamin E, which play an important role in scavenging the toxic intermediate of incomplete oxidation. SOD and CAT are the two major scavenging enzymes that remove toxic free radicals *in vivo*. Previous studies have reported that the activity of SOD is low in diabetes mellitus (Vucic et al., 1997 and Feillet-Coudray et al., 1999). A decrease in the activity of these antioxidants can lead to an excess availability of superoxide anion $O_2^{\bullet-}$ and hydrogen peroxide in biological systems, which inturn generate hydroxyl radicals, resulting in initiation and propagation of lipid peroxidation (Kumuhekar and Katyane, 1992). The result of increased activities of SOD and CAT suggest that THC contains a free radical scavenging activity, which could exert a beneficial effect against pathological alterations caused by the presence of $O_2^{\bullet-}$ and $OH^{\bullet}$. The increased activity of SOD accelerates dismutaion of $O_2^{\bullet-}$ to hydrogen peroxide, which is removed by CAT (Aebi, 1984). This action could involve mechanisms related to scavenging activity of THC.

The pathophysiological consequence owing to depletion of GSH has been well studied. The depletion of GSH, GPx and GST promotes generation of reactive oxygen species (ROS) and oxidative stress with cascade of effects thereby affecting functional as well as structural integrity of cell and organelle membranes (Raza et al., 2000). In addition, the induction of SOD activity by THC may attribute to inhibit the generation of active oxygen species from autoxidation of glucose generation from the action of STZ. In this context, other workers also reported a decrease in the activities of these antioxidant enzymes (SOD, CAT, GPx and GST) in the liver kidney of diabetic rats (Anuradha and Selvam, 1993). As the alteration produced in the antioxidant activities indicate the involvement of deleterious oxidative changes, increased activities of the components of this defence system would therefore be important in protection against radical damage. Administration of THC and curcumin increased the activities of GPx and GST in the liver and kidney of diabetic rats. Vitamin C is a potent antioxidant, which widely acts on oxygen free radicals as well as by interaction with vitamin E (Garg and Bansal, 2000). Both the vitamin C and vitamin E significantly decreased in the liver and kidney of diabetic rats. Administration of THC and curcumin increased the vitamin C and vitamin E levels. This indicates that vitamin E is used in combating free radicals and if vitamin C is present, vitamin E levels are preserved. Also vitamin C regenerates vitamin E from its oxidized form. GSH is a major non-protein thiol in living organisms, which treatment with THC increased the GSH content. GSH is the first line of defense against proxidant status (Ahmed et al., 2000). The elevated level of GSH protects cellular proteins against oxidation through glutathione redox cycle and also directly detoxifies ROS. (Yu, 1994). STZ directly generates oxygen free radical, which induces lipid peroxidation (Spinas, 1999 and Bassirat and Khalil, 2000). It is involved in the maintenance of normal cell structure and function, probably through its redox and detoxification reactions. We observed a decrease in GSH in the liver and kidney during STZ diabetic rats. The decrease in the GSH levels represents increased utilization due to oxidative stress (Anuradha and Selvam, 1993). Administration of THC and curcumin increased the content of GSH in the liver and kidney of STZ diabetic rats. Administration of THC increased the activity of antioxidants and may help to control free radical, as THC and curcumin offered protection to cells against oxidative stress by scavenging free radicals (Khopde et al., 2000 and Okada et al., 2001) generated during diabetes (Anusuya and Menon, 2003). The increased levels of free radical scavenging enzymes may act as an added compensation mechanism to maintain the cell integrity and protection against free radical damage.

An improvement of the antioxidant status might result from the above mentioned effects of curcumin on AGE formation, (Sajithlal et al., 1998) but also direct inhibition of free radicals. Curcumin that can scavenge the ROS and inhibit peroxidation of lipids could be useful as preventive agents against diabetes mellitus (Halim Eshart, 2002). The ability of THC increases the activities of antioxidant enzymes in STZ- treated rats implies that THC reactivates the antioxidant defense system, thereby increasing the capacity of anti diabetic activity through the enhanced scavenging of oxy radicals. The results of Sugiyama et al. (1996) implied that the β-diketone moiety of THC exhibits its antioxidative activity by cleaving the C–C bond at the active methylene carbon between two carbonyls in the β-diketone moiety. In addition, THC and curcumin maintain the blood glucose homeostasis, which inturn prevent the autoxidation of glucose by the presence of insulin secretion from the pancreatic □-cells in drug treated diabetic rats. Thus, findings related to THC suggest that it may safely be implicated as an antioxidant agent in addition to its antidiabetic effect.

Conclusion

We conclude that THC has beneficial effects on glucose concentration as well as sequential metabolic correlation between increased glycolysis, decreased gluconeogenesis, increased hydrogen shuttle reactions. It suggests the possible biochemical mechanisms through which THC regulates glucose homeostasis in diabetic condition. THC significantly reduces the level of serum and tissue lipids which are actively raised in diabetic rats. THC has beneficial effect on plasma insulin and blood glucose level. THC possesses antioxidant effect that may contribute to its protective action against lipid peroxidation and enhancing effect on cellular antioxidant defense. THC administration showed more diabetic effective than curcumin on diabetes.

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