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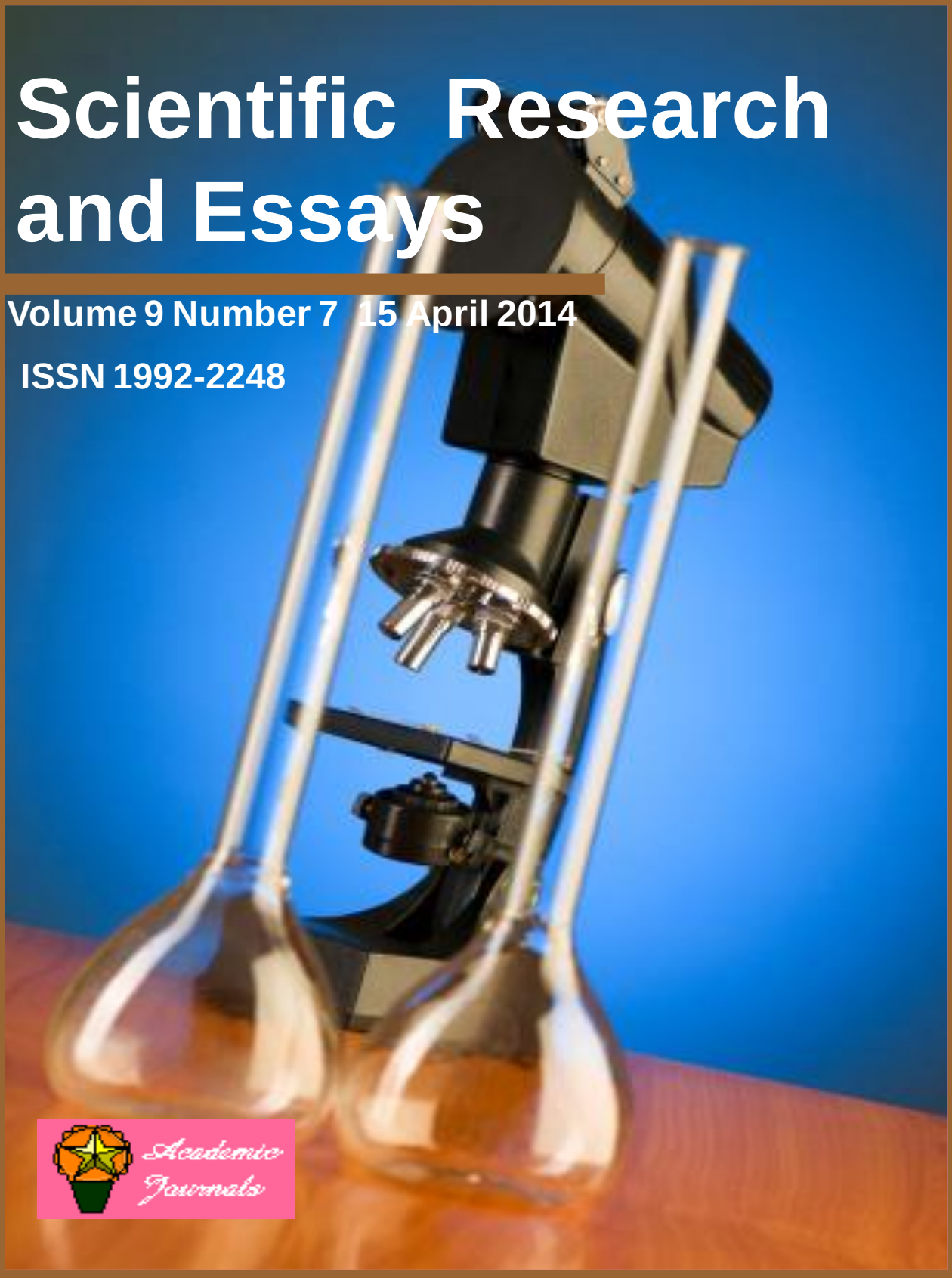

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Scientific Research and Essays

Full Length Research Paper

Failure model and detecting method for MOSFET degradation in DC-DC power converters

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MOSFET is the most commonly used devices in DC-DC power converters, and its performance is important to the prognosis and health management of power. The paper proposes a degradation analysis model for MOSFET in DC-DC power converters. A method for detecting the degradation of MOSFET is also introduced. Simulations have shown that the method can predict deterioration in the performance of MOSFET. The simulation results are good agreement with the theory.

Key words: DC-DC converter, degradation, MOSFET.

INTRODUCTION

DC-DC power converters are widely used in telecommunications equipment, electrical equipment, control equipment, and so on, because they are light, small, thin, and low-cost (Rosas-Caro et al., 2010; Julio Cesar Rosas-Caro et al., 2012). Moreover, DC-DC power is a main component of electronic systems. However, the use of DC-DC power restricts the reliability of electronic systems and directly affects the working status of the entire electronic systems in other aspects such as accuracy and stability. According to statistics, electrolytic capacitors and MOSFETs have a higher degradation rate than other components in DC-DC power (Pang and Pong, 2010). In-depth studies have been conducted on the failure of aluminum electrolytic capacitors, discussing such problems as early failure, the failure mode and the failure mechanism, and the course of deterioration. Considering the impact of the parameters of the working environment (such as temperature, voltage, current, frequency, etc.), some researchers have analyzed the impact of the main parameters of aluminum electrolytic capacitors (such as capacitance, loss angle, leakage current, ripple current, etc.) on its life (Braham et al., 2010; Abdennadher and Venet, 2010; Buiatti et al., 2010; Sun et al., 2010). In the case of MOSFETs, several methods have been proposed to detect faults in MOSFET, for example, short-circuit and open-circuit faults. Previous work on MOSFETs has focused primarily on reliability designs (Azoui et al., 2011), predicting the remaining useful life of MOSFETs using off-line accelerated aging tests (Smet et al., 2011), and developing degradation models based on accelerated life tests (Oukaour et al., 2011).

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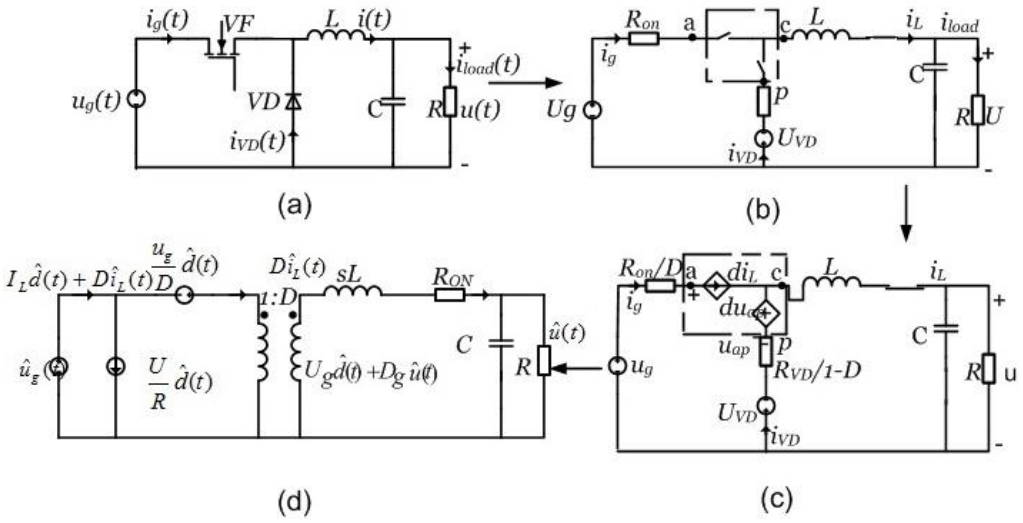

Figure 1. Equivalent Circuit Diagram of a Buck Converter: (a) ideal, (b) non-ideal, (c) large signal averaged model, (d) small signal circuit model.

With the development of technology, a novel technology called Prognostics and Health Management (PHM) has recently been attracting more and more attention. Many papers use on-line monitoring technology. Articles have been written proposing the use of algorithms to extract features to monitor MOSFETs and IGBTs in real time (Ginart et al., 2008). An online non-intrusive method of obtaining the degradation state of MOSFETs based on the Volterra series has been proposed (Wu et al., 2014); however, these methods are complex. In this paper, a failure model for MOSFET is presented and a simple method for estimating degradation of MOSFET in DC-DC power converters is proposed.

MODEL

The equivalent circuit diagram for a DC-DC Buck converter is shown in Figure 1. To achieve the ideal state (as shown in Figure 1(a)), it is possible to obtain transfer functions between the input and output of the converter (Chen, 2010).

The transfer function is as follows:

$$G_{ug}(s) = \left.\frac{\hat{u}(s)}{\hat{u}_g(s)}\right|_{\hat{d}(s)=0} = D\frac{R // \frac{1}{sC}}{sL + R // \frac{1}{sC}} = \frac{R}{LCRs^2 + Ls + R} = \frac{K_1'(\omega_0')^2}{s^2 + 2\zeta'\omega_0' s + (\omega_0')^2} \quad (1)$$

where K_1', ω_0', ξ' represent the amplification, corner frequency, and damping ratio, respectively:

$$K_1' = D \quad (2)$$

$$\omega_0' = \sqrt{\frac{1}{LC}} \quad (3)$$

$$\xi' = \frac{1}{2R}\sqrt{\frac{L}{RC}} \quad (4)$$

The MOSFET equivalent circuit consists of an ideal switch connected in a series with a resistance (Ron), as shown in Figure 1(b), while Figure 1(c) is the Buck converter large signal averaged model. The ideal switch and diode are replaced by a dependent current and voltage sources, respectively. The current of i_g can be expressed as Equation (5) when the MOSFET is turned on.

$$i_g = i_L \approx I_L \quad (5)$$

The effective value of i_g is:

$$I_{grms} = \sqrt{\frac{1}{T_s}\int_0^{DT_s} i_g^{\,2} dt} = \sqrt{D} I_L = \frac{I_g}{\sqrt{D}} = \frac{\sqrt{D}}{1-D} I_{VD} \quad (6)$$

The power loss of MOSFET when turned on is obtained using following equation:

$$P_{R_{on}} = R_{on} I_{grms}^2 = \frac{R_{on}}{D} I_g^2 = D R_{on} I_L^2 \quad (7)$$

Therefore, it is well known that the equivalent resistance (Ron) is Ron/D, which is equivalent to DRon in the

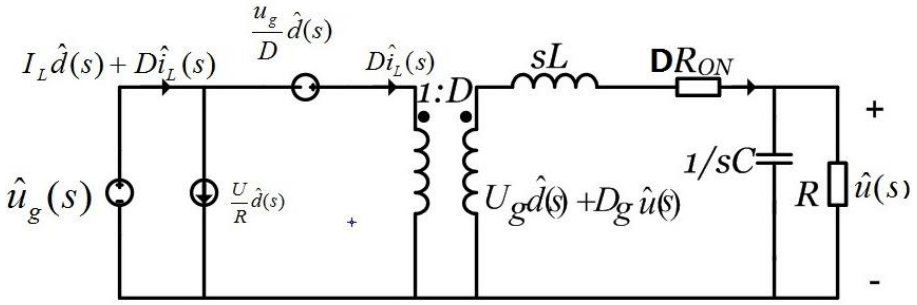

Figure 2. Small signal equivalent circuit diagram of the non-ideal Buck converter in the s domain.

inductor branch based on the energy conserved, according to Equation (7).

Methods

According to Figure 1(d), the small signal equivalent circuit diagram of the non-ideal Buck converter in the s domain has been established (Figure 2).

It is well known that the transfer functions can be expressed as follows:

$$G_{ug}(s)=\left.\frac{\hat{u}(s)}{\hat{u}_g(s)}\right|_{\hat{d}(s)=0}=D\frac{R//\frac{1}{sC}}{sL+DR_{ON}+R//\frac{1}{sC}}=\frac{\frac{D}{LC}}{s^2+(\frac{L+DR_{ON}RC}{RLC})s+\frac{DR_{ON}+R}{RLC}}$$

$$=\frac{K_1{\omega_0}^2}{s^2+2\xi\omega_0 s+{\omega_0}^2} \quad (8)$$

where K_1, ω_0, ξ represent the amplification, corner frequency and damping ratio, respectively:

$$K_1=D\frac{R}{R+DR_{ON}} \quad (9)$$

$$\omega_0=\sqrt{\frac{DR_{ON}+R}{LCR}}=\sqrt{\frac{1}{LC}+\frac{DR_{ON}}{LCR}} \quad (10)$$

$$\xi=\frac{L+CRDR_{ON}}{2\sqrt{LCR(R+DR_{ON})}} \quad (11)$$

Now, adding an excitation signal, the output will change. While the MOSET degradation occurs, the resistance Ron will increase, causing the output to change. The state of MOSFET through the output can be obtained.

$$U(s)=G_{ug}(s)R(s)=\frac{K_1{\omega_0}^2}{s^2+2\xi\omega_0 s+{\omega_0}^2}\bullet\frac{K_2}{s} \quad (12)$$

The u(t) can be obtained using the Laplace inverse transformation, which is shown as:

$$u(t)=\frac{K_1K_2}{\omega_0}[1-\frac{e^{-\sigma t}}{\sqrt{1-\xi^2}}\bullet\sin[\omega_d+\varphi]] \quad (13)$$

where ω_d, σ, φ can be expressed as:

$$\omega_d=\omega_0\sqrt{1-\xi^2}$$

$$\sigma=\xi\omega_0$$

$$\varphi=\arctan\frac{\sqrt{1-\xi^2}}{\xi}=\arccos\xi$$

Comparing Equations (2 to 4) and Equations (9 to 11), it is clear that these parameters will change with the degradation of MOSFET. Therefore, it is clear that the state of MOSFET can be obtained by detecting the transient response signal. From the response signal, the Ron is gained. According to the relationship between the degradation state (useful life) and the Ron (Celaya et al., 2012), the state can be detected. The method for detecting the degradation of MOSFET is shown in Figure 3.

RESULTS AND ANALYSIS

In order to verify the validity of the method, MOSFETs in different degrees of degradation are selected to be set in the Buck converter, and the output signals are shown in Figure 4. The results indicate that the Ron increases with the degradation of MOSFET, causing the transient response signal to change. Ron1 expresses the state before degradation, and Ron8 expresses the failure state. From the information of the output signals, including the amplification, corner frequency and damping ratio, the degree of degradation of MOSFET can be judged. By monitoring the changes of the feature signals, it is easy to indirectly measure the degree to which MOSFET has deteriorated. The relationship between the max amplitude and the Ron can be expressed, as shown in Figure 5.

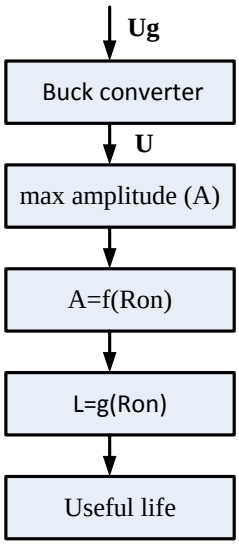

Figure 3. Chart on the method for detecting the degradation of MOSFET.

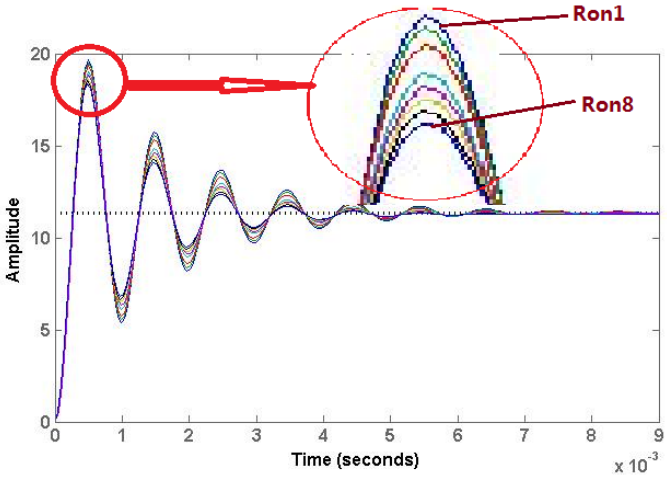

Figure 4. The transient response signal with the Ron increase caused by degradation of MOSFET.

According the relationship shown in Figure 5, the Ron can be gained, and the degradation of MOSFET can be predicted by taking advantage of the relation of L=g(Ron) (Celaya et al., 2012).

Conclusions

The simulation and the test results indicate that degradation process of MOSFET leads to an increase in the resistance. The change in the Ron is difficult to measure; it is easy to obtain the change in the response signal caused by the Ron. The degree of degradation is determined by analyzing the response signal collected in the test. Based on the trend of the changes, the remaining useful life of MOSFET in a DC-DC converter can be accurately predicted.

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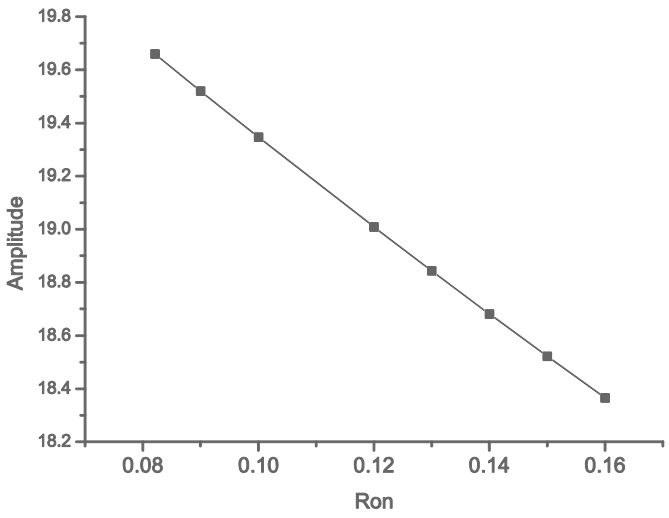

Figure 5. The relationship between the max amplitude and the Ron.

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Conflict of Interests

The author(s) have not declared any conflict of interests.

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Scientific Research and Essays

Full Length Research Paper

Performance assessment of transferred irrigation management: Case study of Düzce Irrigation District in Turkey

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In this study, physical and financial performance criteria of transferred irrigation management of Düzce Irrigation District were evaluated between 2006 and 2012. Physical and financial performances are irrigation ratio and sustainability of irrigated land, and cost recovery ratio, maintenance expenditure to revenue ratio, operational cost per unit area, total cost per personnel employed on water delivery, revenue collection performance and service area per personnel, respectively. The analysis results indicated that irrigation ratios were between 12.8 to 23.2% while sustainability of irrigated land rates were between 1.33 to 2.40 for the studied years. On the other hand, cost recovery ratio and revenue collection performance values were changed between 56.4 to 89.4 and 70.9 to 93.2%, respectively. Moreover, maintenance expenditure to revenue, operational cost per unit area, total cost per person employed on water delivery and service area per personnel had between 4.8 to 24.4%, 111.3 to 183.9 US$ ha^{-1}, 7288.5 to 13168.8 US$ ha^{-1} and 116.9 to 234.9%, respectively. As a conclusion, it was stated that transferred irrigation management for Düzce Irrigation District does not have enough financial and physical performances and needs recovery.

Key words: Sustainability, irrigation ratio, operating cost, water delivery, Düzce.

INTRODUCTION

Water is a precious resource for agricultural production and unavoidable component for food security. Therefore, water scarcity and abuse create a serious threat to life and sustainable development. Increasing yield in many places to sustain food production depends on irrigation, as water is the limiting factor around the world. For that, water protection and development are considerable for irrigation opportunity (Sampathkumara et al., 2012).

Irrigation is the most important factor in agricultural development strategy in Turkey. This importance is growing steadily considering dependence of the country's industry on agriculture. Water sources decrease day by day in Turkey because of increasing population as in the whole of Middle East. It is not only due to industrialization but also with global warming and the lack of uniformity in the distribution resources within the country, it increases the severity of this problem quickly (Çakmak and Aküzüm, 2006).

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Figure 1. Location of Düzce Area in Turkey.

A total of 28.05 million ha is arable out of the total area of 78 million ha in Turkey. A total of 25.75 million ha of agricultural area can be irrigated. Economically, Turkey's potential surface and groundwater resources are sufficient for irrigating a land area of 8.50 million ha; 4.89 million ha of which was opened to public and private irrigation presently. 94% of the irrigated area is irrigated by means of open canal systems while 6% of that uses pressurized irrigation systems in Turkey (Anonymous, 2008).

In Düzce Area, 36% in the total irrigation area of 22,250 ha is irrigated. Düzce Irrigation District uses 78% of the total irrigated area. Between 5 and 10% of the irrigated area is irrigated by means of pressurized irrigation systems in Düzce Irrigation District (Özmen, 2013).

During the last two decades, there has been an increasing amount of effort to transfer the management of irrigation schemes from government organizations. However, irrigation management transfers that are initiated by governments have had poor management performances, lack of operational and maintenance funds and/or very low water charge collection from the farmers (Kloezen and Samad, 1995). Therefore, some of performance analyses such as physical and financial performances need to be searched in the transfer irrigation management.

Dorsan et al. (2004) studied about some physical, economic and institutional performance criteria of transferred irrigation schemes of Lower Gediz Basin for pre and post-transfer periods in Turkey. Researchers found out that all performance criteria was changed positively but the most positive change has occurred in the collection of irrigation fee (Yercan et al., 2009). Similar results were obtained by Nalbantoğlu and Çakmak (2007) in the Central Anatolia Region.

Şener et al. (2007) assessed the performance of Hayrabolu Irrigation Scheme of the Thrace district in Turkey. They found economic performance indicators showed that the scheme had a serious problem about the collection of water fees. Additionally, it was achieved that physical performance, evaluated in terms of irrigation ratio and sustainability of irrigated land, were poor in this study. However, Şener (2012) pointed out that the irrigation management transfer program increased the system performance and the schemes have become more self-sufficient under the management of Water User Associations (WUAs) in another study in the same region.

In this sense, such investigation has so far not been done in Düzce Area. Hence, the aim of this study is to evaluate physical and financial performance criteria of Düzce Irrigation District using transferred WUAs from State Hydraulic Waters (SHW) for the years between 2006 and 2012 in the Düzce area localized in the northern Turkey.

MATERIALS AND METHODS

In this research, Düzce Irrigation District serving under the fifth SHW regional directorate after the year of 2005, which is located in Düzce Area in Turkey, was examined (Figure 1). Annual average precipitation for the last 40 years in the studied area is 814 mm.

Table 1. Long term and annual rainfall (mm) between 2005 and 2012 in studied area.

Months	Long term average rainfall (Last 40 years)	2006	2007	2008	2009	2010	2011	2012
January	82.6	66.2	100.8	76.6	66.4	101.2	68.4	59.1
February	70.1	54.7	28.4	17.2	86.2	105.3	21.2	119.1
March	71.6	48.7	92.2	89.4	90.9	97.7	104.5	84.6
April	59.6	7.2	34.5	13	48.7	67.7	88.3	39.6
May	61	39.4	56.5	66	25	65.7	39	74.6
June	57.2	33.2	84.4	13	37.4	96.6	61.3	38.4
July	44.2	8.8	28.8	22.8	94.8	7.4	18.7	23.1
August	52.8	4.2	34.2	0.0	9	2	33.8	90.6
September	48.3	101.9	14.4	120.2	149.3	69.1	17.6	0.4
October	83.5	34.2	67.2	73	57.4	137.2	64.2	51.1
November	84.5	67.2	85.8	46.4	56.3	10.5	22.6	44.8
December	98.7	61.3	58.2	90.2	77.5	120.8	62.1	129.5

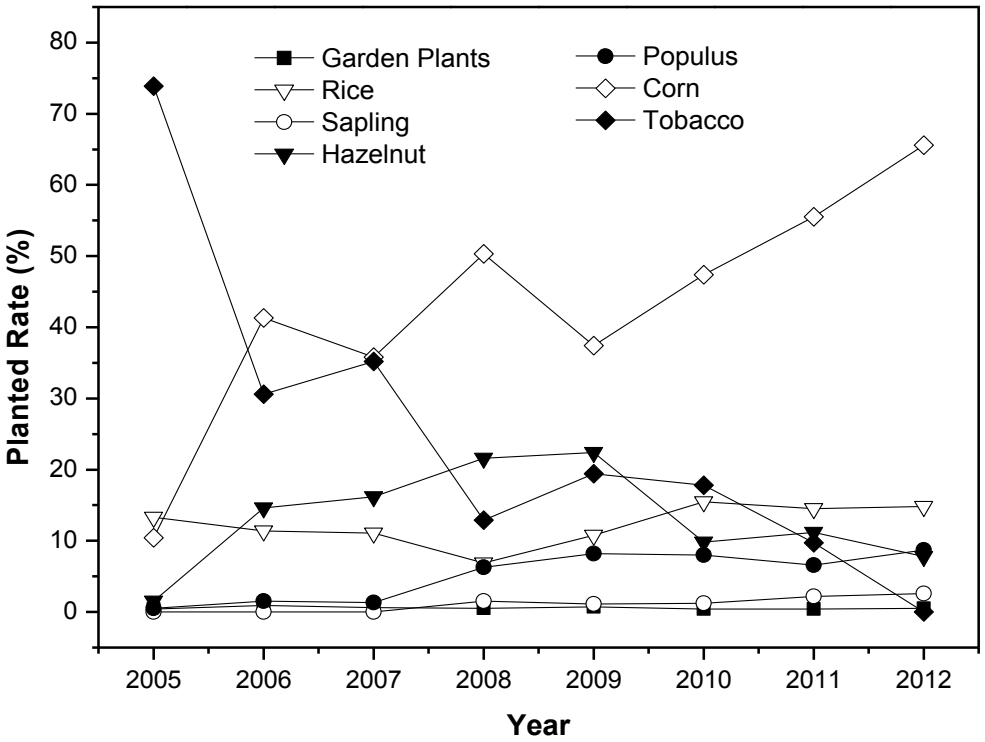

Figure 2. Planted rate in the Düzce area between 2005 and 2012.

Monthly average precipitations for the long term and studied years are given in Table 1 (Anonymous, 2013).

In the studied area, hazelnut, corn, populous, sapling, tobacco and garden plants are generally planted (Anonymous, 2012a; Figure 2). However, tobacco planting rate is decreased from 2005 to 2012 while corn planted rate is increased in the same period but others stayed the same thanks to policy of government.

Düzce Irrigation District was assessed for their physical and economic performance criteria. The analysis is based on time series. Time series covering a period of 7 years were collected to measure any change in performance over time at the scheme level. Performance criteria (Malano and Burton, 2001) are given in the Table 2. Related data for this research were taken from records of SWH fifth Regional Directorate and Düzce Irrigation District Presidency (Anonymous, 2012b). The currency unit was converted from Turkish Liras to American Dollars using the Central Bank of Turkish Republic's foreign exchange rate.

RESULTS AND DISCUSSION

Irrigation ratios of Düzce Irrigation District between 2006 and 2012 according to the records of the SWH in the

Table 2. Selected performance indicators**.**

Activity area	Performance indicator	Data required
Physical performance	Irrigation ratio	Irrigated area/Irrigation area
	Sustainability of irrigated area	Irrigated area/Initial irrigated area
Financial performance	Cost recovery ratio	Total revenue collected from water users/Total management, operation and maintenance cost
	Maintenance expenditure to revenue ratio	Total maintenance expenditure/Total revenue collected from water users
	Operating cost per unit area ($ ha^{-1})	Total management, operation and maintenance cost/Total command area serviced by the system
	Total cost per person employed on water delivery ($/person)	Total cost of management, operation and maintenance personnel/Total number of people employed
	Revenue collection performance	Total service revenue collected/Total service revenue due
	Service area per personnel (ha/person)	Total command area serviced by the system/ Total number of management, operation and maintenance staff

Table 3. Irrigation Ratios of Düzce Irrigation District.

Years	Irrigated area (ha)	Irrigation area (ha)	Irrigation ratios (%)	Sustainability irrigated area rate
2006	1644.6	11000.0	15.0	1.55
2007	1717.5	11000.0	15.6	1.62
2008	2547.5	11000.0	23.2	2.40
2009	1934.0	11000.0	17.6	1.83
2010	1766.7	11000.0	16.1	1.67
2011	1712.2	11000.0	15.6	1.62
2012	1403.3	11000.0	12.8	1.33

Table 4. Cost recovery ratio of Düzce Irrigation District.

Years	Total revenue collected from water users (US$)	Total maintenance operating management cost (US$)	Cost recovery ratios (%)
2006	161838.5	183062.9	88.4
2007	206519.2	305310.0	67.6
2008	286969.5	320984.4	89.4
2009	180440.9	258229.2	69.9
2010	211007.3	265491.3	79.5
2011	184900.6	264219.6	70.0
2012	145461.8	258078.7	56.4

study area are given in Table 3. Ratios are similar to results of works by Yercan et al. (2004) but are mostly lower than study reported by Çakmak (2002) and Şener et al. (2007) due to regional conditions.

Sustainability irrigated area rates were changed between 1.00 to 2.40 during studied years. The highest rate was in the year 2008 with value of 2.40 because of higher irrigated area comparing with initial irrigated area (Table 3). The reasons for lower values of sustainability irrigated area rates could be due to land degradation by drainage problems and misuse of land or management problem. Study results are similar to values of study by Dorsan et al. (2004).

Cost recovery ratio was maximum in the year 2008 with 89.4% (Table 4). Data shows that the total revenue collected from water users were insufficient to cover the maintenance operation management costs in this study. However, Beyribey (1997) pointed out that average cost recovery ratio of the country was 65%. Hence, cost recovery ratio results of this study seem acceptable but

Table 5. Maintenance expenditure to revenue of Düzce Irrigation District.

Years	Total maintenance cost (US$)	Total revenue collected from water users (US$)	Maintenance expenditure to revenue ratio (%)
2006	31874.1	161838.5	19.7
2007	26421.5	206519.2	12.8
2008	25237.5	286969.5	8.8
2009	8635.7	180440.9	4.8
2010	18965.3	211007.3	9.0
2011	45106.0	184900.6	24.4
2012	21428.7	145461.8	14.7

Table 6. Operating cost per unit area of Düzce Irrigation District.

Years	Total maintenance operating management cost (US$)	Irrigated area (ha)	Operating cost per unit area (US$ ha^{-1})
2006	183062.9	1644.6	111.3
2007	305310.0	1717.5	177.8
2008	320984.4	2547.5	126.0
2009	258229.2	1934.0	133.5
2010	265491.3	1766.7	150.3
2011	264219.6	1712.2	154.3
2012	258078.7	1403.3	183.9

Table 7. Cost per personnel of Düzce Irrigation District.

Years	Total cost of maintenance-operating-management personal (US$)	Total number of people employed person	Cost per personnel (US$/person)
2006	42428.7	5	8485.7
2007	72884.6	10	7288.5
2008	108515.6	11	9865.1
2009	124198.1	11	11290.7
2010	131688.0	10	13168.8
2011	109891.7	9	12210.2
2012	126706.7	10	12670.7

should be recovered.

The highest maintenance expenditure to revenue ratio was obtained in the year 2011 with 24.4% (Table 5). For this study, the results are higher compared with study of Nalbantoğlu and Çakmak (2007). However, revenue collected from water users seems sufficient to maintenance costs during the studied years (Table 5).

Regarding the operational-cost per unit irrigation area, the highest cost per unit area was obtained from the year of 2012 with US$ 183.9 ha^{-1} (Table 6). Values are higher than the studies done before (Çakmak et al., 2010). Total maintenance operating management costs are higher according to irrigated area in the study area.

The highest cost per personnel was provided in the year 2010 with 13168.8 USD per person (Table 7). Labour costs are generally higher for all year in the study years.

The highest revenue collection performance was estimated for the year 2007 with 93.2% (Table 8). Revenue collection performance values are mostly over 80% during the studied years except last year. Similar results were reported by Yercan et al. (2009). Obtaining results showed that revenue collection performances seem sufficient but not enough during the years in this study.

The highest values of service area per personnel were found in the year 2006 with 211.8 ha $person^{-1}$ (Table 9). The number of labour for an irrigation scheme should be less than 3 per 1000 ha of irrigated land for an efficiency consideration (Yercan et al., 2009). However, the current data analysis implies that more than enough people are employed for the study area (Table 9). Therefore, service areas per personnel values of the study area are higher for that reason.

Table 8. Revenue collection performance of Düzce Irrigation District.

Years	Total collected water fee from the users (US$)	Total water fee to be collected (US$)	Revenue collection performance (%)
2006	161838.5	187412.6	86.4
2007	206519.2	221538.5	93.2
2008	286969.5	342187.5	83.9
2009	180440.9	218831.2	82.5
2010	211007.3	243333.3	86.7
2011	184900.6	215476.2	85.8
2012	145461.8	205056.2	70.9

Table 9. Service area per personnel of Düzce Irrigation District.

Years	Irrigated area (ha)	Total number of personnel employed in operation and maintenance	Service area per personnel (ha/person)
2006	1644.6	7	234.9
2007	1717.5	12	143.1
2008	2547.5	13	196.0
2009	1934.0	13	148.8
2010	1766.7	12	147.2
2011	1712.2	11	155.7
2012	1403.3	12	116.9

Conclusion

The results of this study showed that total revenue collected from water users were not sufficient to meet the maintenance operation management costs but were generally sufficient to meet maintenance cost during the studied years. Moreover, operating costs per unit irrigation area and cost per personnel were found higher in the ending of studied years. However, revenue collection performance results were over 70%, which seems sufficient. Concerning service area per personnel, it can be explained that all irrigation services have excess employed personnel thanks to distribution network of irrigation scheme. Conclusively, physical and financial performances need further studies.

Conflict of Interests

The author(s) have not declared any conflict of interests.

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Scientific Research and Essays

Full Length Research Paper

Computational Fluid Dynamics (CFD) simulation to analyze the performance of tube-in-tube helically coiled of a heat exchanger

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This work deals with a comparative performance study of two different helically coiled heat exchangers with two and three helical coils through a Computational Fluid Dynamics (CFD) simulation for heat transfer characteristics. The helically coiled heat exchangers are typical industrial equipments found in process applications, such as: chemical, food, energy, electronics, environmental, spatial, and cryogenic. Numerical studies were performed with the assistance of a commercial computational fluid dynamics package (ANSYS-CFX v12). Simulations were performed using various temperatures (hot fluid inlet temperature of 25, 30, 35 and 40°C) and the inlet cold fluid temperature is 20°C. Results indicated that the performance of both heat exchangers for the temperature 25°C (hot fluid inlet) was quite similar, but for the temperature 40°C (hot fluid inlet), the heat exchanger with three turns was more efficient than another exchanger (two turns). It was shown that the performance could be increased by increasing the hot fluid inlet temperature with two and three helical coils.

Key words: Computational Fluid Dynamics (CFD) analysis, heat exchanger, helically coiled performance, number of helically coils.

INTRODUCTION

The helically coiled heat exchangers, also called TTHC (tube-in-tube helically coiled), are typical industrial equipments found in process applications, such as: chemical, food, energy, electronics, environmental, spatial and cryogenic (Kumar et al., 2006). Applications often involve heating or cooling of a fluid to evaporate or condense another fluid. The helically coiled heat exchangers are also used in not traditional processes as sterilization, pasteurization, concentration, crystallization, separation (distillation) etc.

Centrifugal forces acting on the fluid during the passage in the helical coil and due to the curvature of helical coils can generate a secondary fluid flow that has a circular motion; the consequence of this circular motion is that the fluid particle moves into the core tube, the temperature gradient in the pipe section is reduced and the heat exchange is increased. This mechanism for exchanging additional heat, perpendicular to the fluid

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Figure 1. Industrial helically coiled heat exchanger (JMS Equipamentos, 2012).

motion is only found in heat exchangers curved tubes (Pimenta, 2010).

Figure 1 is shows an example of industrial helically coiled heat exchanger. Several authors have studied TTHC applications because of its flexibility and efficiency. Some CFD simulation of TTHC had been done for several boundaries conditions and had used actual models to make a comparison with a virtual analysis model (Sahoo et al., 2002; Sahoo et al., 2003; Jayakumar et al., 2008). Also, performance analysis of different TTHC were done and it highlighted that construction and geometry parameters influence significantly in the heat exchanger coefficients (Salimpour, 2009; Abdel-Aziz et al., 2010; Genic et al., 2012; Zhou and Chen, 2012).

Computational numerical simulation on a helically coiled heat exchanger performance has been done and compared to results measured in laboratory experiments (Rennie and Raghavan, 2006; Kumar et al., 2008; Munoz and Adanades, 2011; San et al., 2012; Li et al., 2012).

Computational numerical simulation can be used to study the fluid flow and heat transfer for a wide variety of engineering equipment. In this study, we use Flow Simulation to determine the efficiency of a counter-flow heat exchanger and to observe the temperature inside of it. With Flow Simulation the determination of heat exchanger efficiency is straightforward and by investigating the temperature patterns, the design engineer can gain insight into the physical processes involved, thus giving guidance for improvements to the design (Solidsworks Flow Simulation, 2009).

Purandare and Gupta (2012) carried out a comparative analysis of the different correlations given by different researchers for helical coil heat exchanger. They observed that the helical coils are efficient for low Re (laminar regime). Also the ratio of tube diameter to coil diameter should be large enough for large intensities of secondary flows inside the tubes.

An experimental investigation of the mixed convection heat transfer in a coil-in-shell heat exchanger is reported for various Reynolds number, various tube-to-coil diameter ratios and dimensionless coil pitch was carried out by Ghorbani et al. (2010) where the purpose was to assess the influence of the tube diameter, coil pitch, shell-side and tube-side mass flow rate over the performance coefficient of vertical helical coiled tube heat exchanger.

A numerical investigation of the heat transfer from vertical helically coiled tubes in a cylindrical shell was carried out by Mirgolbabaei et al. (2011). The particular difference in this study compared with other similar studies is the boundary conditions for the helical coil. Constant temperature (80°C) was considered for inlet flow to the coil and the inlet temperature of the shell-side fluid was 20°C. Cold water enters the shell-side at the bottom (inlet mass flowrate boundary condition) and leaves at the top (outlet boundary conditions). The shell-side mass flow rates of water were in the range 0.03 to 0.09 kg/s (the coil-side flow regime is laminar). The inner and outer walls of the pipe were defined as coupled for energy transfer from the hot fluid (inside the pipe) to the cold fluid (in the shell). For momentum equation, the walls were treated as no-slip ones. The inner and outer wall of the shell were taken as no-slip adiabatic ones. The influence of the tube diameter, coil pitch and shell-side mass flow rate on shell-side heat transfer coefficient of the heat exchanger was reasonably demonstrated.

This work deals with a comparative performance study of two different helically coiled heat exchangers with two and three helical coil through a computational simulation. CFD computations have been done for hot water which flows in helical copper coil, with cold water flowing

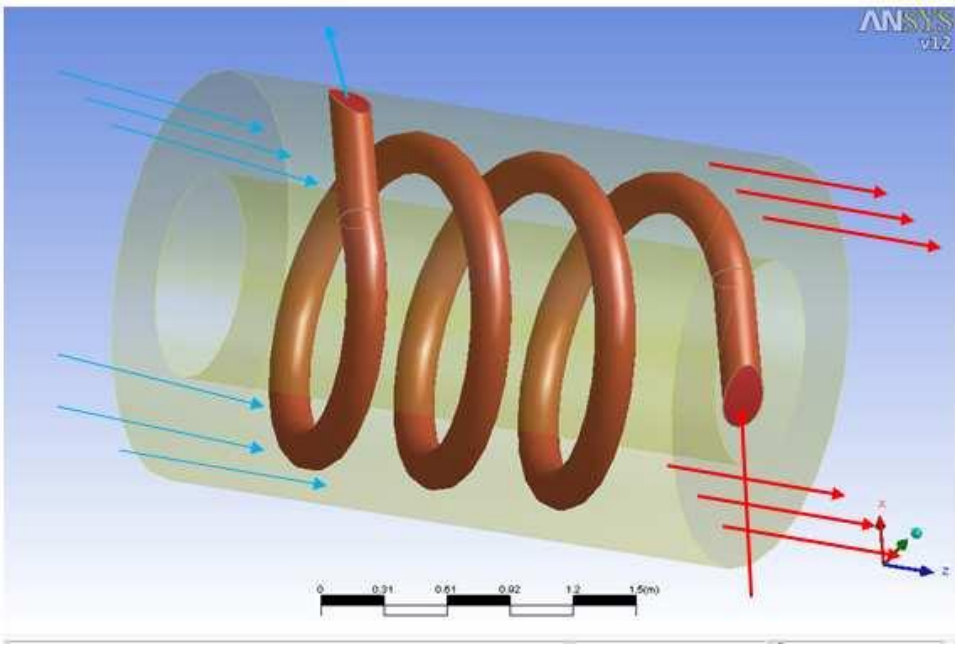

Figure 2. Schematic of the helically coiled heat exchanger.

Table 1. Fluids characteristics.

Properties	Values
Density [kg/m^3]	997
Specific heat capacity [J/kg.K]	4,187.7
Reference pressure [atm]	1
Reference temperature [°C]	20
Thermal conductivity [W/m.K]	0.6069
Dynamic viscosity [kg/m.s]	8.899×10^{-4}

Table 3. Heat exchanger with two helical coils – characteristics.

Characteristics	Values
Coil inner diameter [m]	0.196
Coil outer diameter [m]	0.2
Coils distances [m]	0.7
Coil angle [°]	79.6
Bigger cylinder diameter [m]	2
Smaller cylinder diameter [m]	1
Heat exchanger length [m]	3
Total coil length [m]	11

outside two concentric cylinders in the opposite direction.

METHODS

Simulations were performed using various temperatures (hot fluid inlet temperature of 25, 30, 35 and 40°C) and the inlet cold fluid temperature is 20°C. For momentum equation, the walls were treated as no-slip ones. The inner and outer wall of the shell were taken as no-slip adiabatic ones. Thermal energy transfer is modelled for a copper coil that carries hot water and has externally cold water passage, which has the fluid refrigeration function. Hot fluid inlet velocity was 0.01 m/s and Cold fluid inlet velocity was 0.1 m/s where the coil-side flow regime is laminar (Reynolds number corresponding to these velocities flow were 2,562 and 425 respectively). The inner and outer walls of the pipe were defined as coupled for energy transfer from the hot fluid (inside the pipe) to the cold fluid (in the shell).

Figure 2 shows the helical copper coil arrangement described in which it is possible to see the outside of two concentric cylinders with coolant water passing between them.

The cold fluid passing between the cylinders is represented by the blue arrows, the orange arrows in the coaxial direction represent cold fluid upon heating and the red arrows in the radial direction (into the coil) represent the hot fluid that will be cooled.

A computer simulation to evaluate the thermal exchange and the fluids velocity during the process was done with ANSYS CFX v12 CFD software (ANSYS CFX, 2009). Several relevant characteristics about the heat exchangers dimensioning (physical dimensions of heat exchanger) and about working fluids are presented in Tables 1, 2, 3, and 4 (Pimenta, 2010).

The dimensions that were used in this simulation are compatible with the actual heat exchanger dimension normally found in industries. Some assumptions must be considered to perform the simulation and discuss results throughout the work.

The heat exchangers analyzed have counter-current flow because the performance is better compared to parallel-current heat exchangers. The water is used for both hot and cold fluids, and the metallic material of the heat exchanger is copper. The system is considered permanent and incompressible-fluid, as seen in Table 2. The criterion of convergence used for the variables velocity (u, v, w) and temperature was 10^{-4} RMS (residual mean

Table 2. Criterion of incompressibility.

Sound velocity in the fluid [v = 1,400 m/s]	v_{fluid} (m/s)	Mach number
Hot fluid inlet velocity	0.01	Ma = 0.0000071 < 0.3
Cold fluid inlet velocity	0.1	Ma = 0.000071 < 0.3

Table 4. Heat exchanger with three helical coils – characteristics.

Characteristics	Values
Coil inner diameter [m]	0.196
Coil outer diameter [m]	0.2
Coils distances [m]	0.6
Coil angle [degree]	82
Bigger cylinder diameter [m]	2
Smaller cylinder diameter [m]	1
Heat exchanger length [m]	3
Total coil length [m]	15

Table 5. Hot/cold fluid domain – mesh refining.

Domain	Nodes	Elements
Cold	250,931	932,592
Hot	147,665	467,159
Total	398,596	1,399,751

square) and the maximum number of iterations was 200.

The three-dimensional computational domain was modelled using Hexahedral meshes for both models are shown in Table 5. The complete domain consists of 932,592 elements (cold domain) and 42,602 elements (hot domain). A grid independence test was performed to check the validity of the quality of the mesh on the solution. Further refinement did not change the result by more than 2% which is taken as the appropriate mesh quality for computation.

The effectiveness concept is used for heat exchanger efficiency calculation. The effectiveness (ε) may be defined as the ratio of real heat transfer rate in the heat exchanger (q real) and the maximum possible one (q max), such as Equation (1) (Bergman et al., 2011).

$$\varepsilon = \frac{q_{real}}{q_{\max}} \quad (1)$$

$$q_{real} = C_h - \left(T_{h,i} - T_{h,o}\right) \quad (2)$$

$$q_{\max} = C_{\min} - \left(T_{h,i} - T_{c,i}\right) \quad (3)$$

Equations (2) and (3) present the magnitudes associated with this definition, Equation (1) (Bergman et al., 2011).
Where,
C_h – thermal capacity of hot fluid [kW/°C];
$T_{h,i}$ – temperature of hot fluid inlet [°C];
$T_{h,o}$ – temperature of hot fluid outlet [°C];
$T_{c,i}$ – temperature of cold fluid inlet [°C].

For Equation (3), C_{min} is the less value of C_h, Equation (4), and C_c, Equation (5)

$$C_h = \dot{m}_h - c_{p,h} \quad (4)$$

$$C_c = \dot{m}_c - c_{p,c} \quad (5)$$

Where:
C_c – thermal capacity of cold fluid [kW/°C];
$\dot{m}_h$ – mass flow of hot fluid [kg/s];
$c_{p,h}$ – specific heat of hot fluid [kJ/(kg.°C)];
$\dot{m}_c$ – mass flow of cold fluid [kg/s];
$c_{p,c}$ – specific heat of cold fluid [kJ/(kg.°C)].

For results of heat transfer through the helical coil, the following equations for Reynolds number have been used (Equation 6):

$$\mathrm{Re} = \frac{\rho u d}{\mu} \quad (6)$$

Where:

μ - coefficient of dynamic viscosity (kg/(m.s));
ρ - density of fluid (kg/m^3);
u - mean velocity of flow (m/s);
d - tube diameter (m).

RESULTS AND DISCUSSION

The simulation results with two and three coils were developed in the study cases appointed in 1 and 2, with 25 and 40°C respectively for hot fluid inlet temperature. The results are presented in the diagram of temperatures for several heat exchange sections obtained by computation software for each device.

Heat exchanger with two coils

The heat exchanger with two coils is preliminarily analyzed following exactly the characteristics presented in Table 3. The working fluid is water and its characteristics are verified in Tables 1 and 2.

Study case 1: Inlet temperature of hot fluid at 25°C

Figure 3 shows the temperatures along the heat exchanger with two coils. Temperature homogeneity can

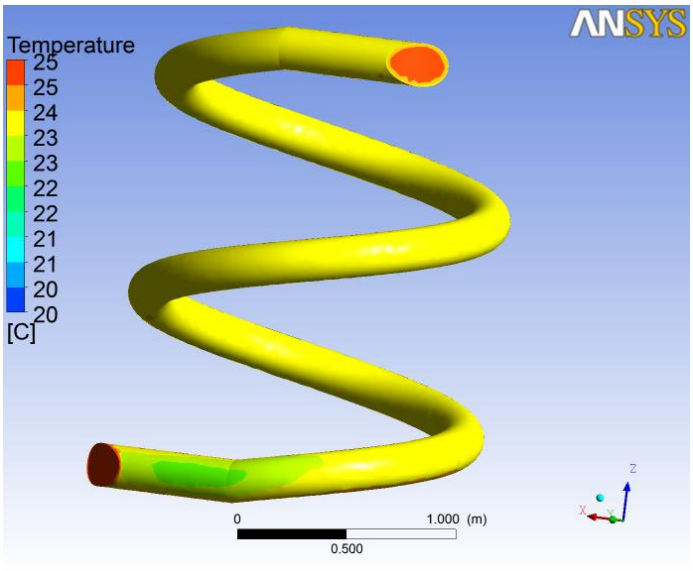

Figure 3. Two coils and hot fluid inlet temperature at 25°C - temperature map.

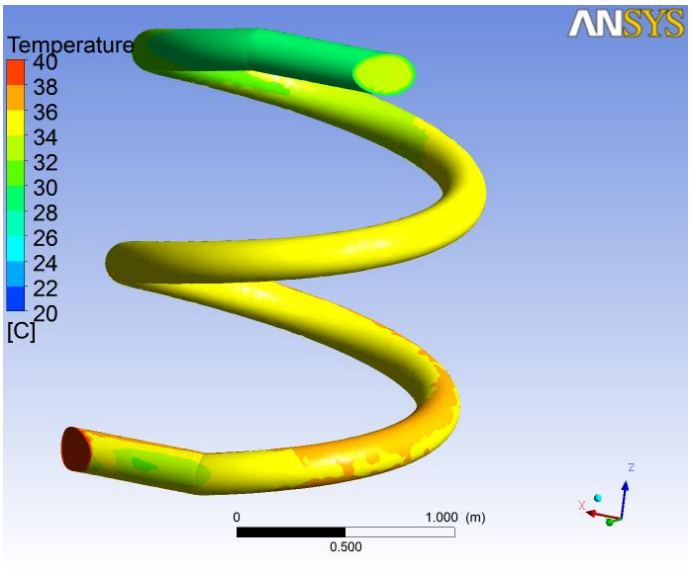

Figure 5. Two coils and hot fluid inlet temperature at 40°C – temperature map.

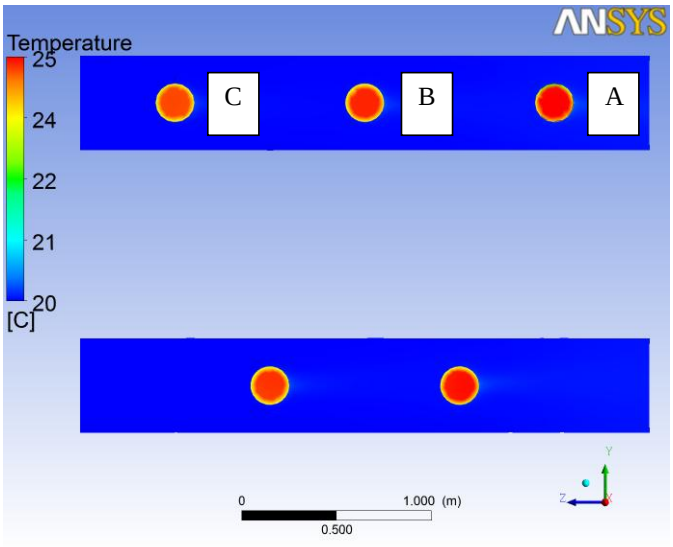

Figure 4. Two coils and hot fluid inlet temperature at 25°C – temperature.

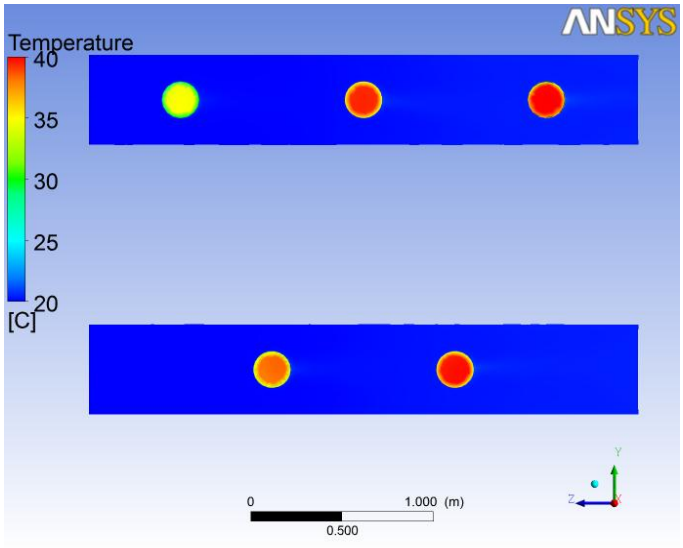

Figure 6. Two coils and hot fluid inlet temperature at 40°C – temperature.

be verified throughout the heat exchanger. It can be explained by the hot fluid temperature very near to cold fluid temperature ($\Delta T = 5°C$).

Figure 4 shows the coil front cuts temperatures in heat exchanger. Obviously the inlet temperature in the point (A) has the largest value and it can be verified to have a gradual reduction of temperature in each section of pipe (B and C) until the lower temperature (point C). The homogeneity of temperature can also be seen in Figure 4 being consistent with Figure 3.

Study case 2: Inlet temperature of hot fluid at 40°C

Figure 5 shows the diagram for temperatures along the coils length. It is verified to exhibit a temperature drop more pronounced in Figure 5 compared to Figure 3. Due to the fact that the hot fluid temperature inlet is higher than study case 1, so, there is a temperature drop more sharply on the first turn. In this case, it has a $\Delta T_{max} = 30°C$.

The results observed shown in Figure 6 are quite similar to the first one in study case 1 (25°C). The system

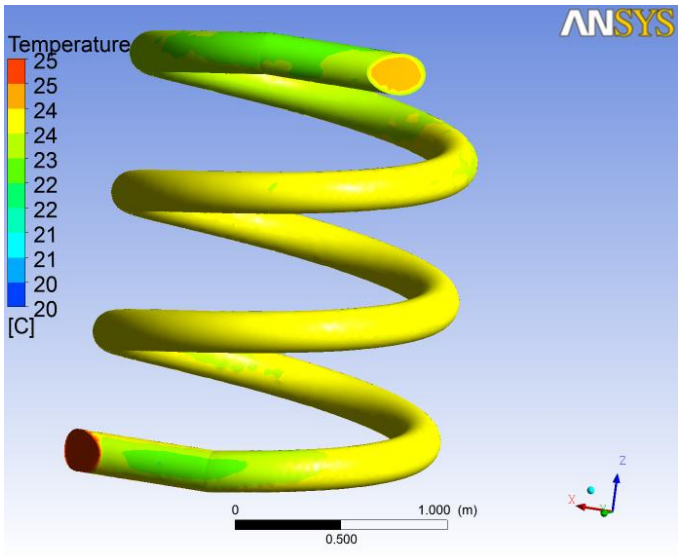

Figure 7. Three coils and hot fluid inlet temperature at 25°C – temperature map.

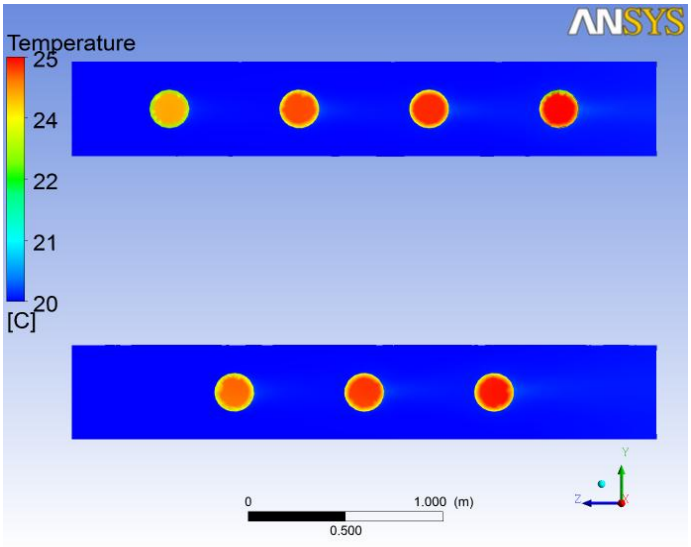

Figure 8. Three coils and hot fluid inlet temperature at 25°C – temperature.

efficiency in study case 1 was lower than the study case 2 and this fact can be explained by the small number of turns which means a smaller area of heat exchange and the temperature of upper hot fluid inlet (40°C). There is not sufficient proper area to achieve the heat exchange.

Heat exchanger with three coils

Figure 7 shows the diagram of temperatures throughout the heat exchanger with three coils.

Table 6. Results comparison for two coils – study cases 1 and 2.

Case	Case 1	Case 2
Hot fluid inlet temperature [°C]	25	40
Efficiency [%]	6.5	33.97

Table 7. Results comparison for three coils – Study cases 1 and 2.

Case	Case 1	Case 2
Hot fluid inlet temperature [°C]	25	40
Efficiency [%]	17.58	77.7

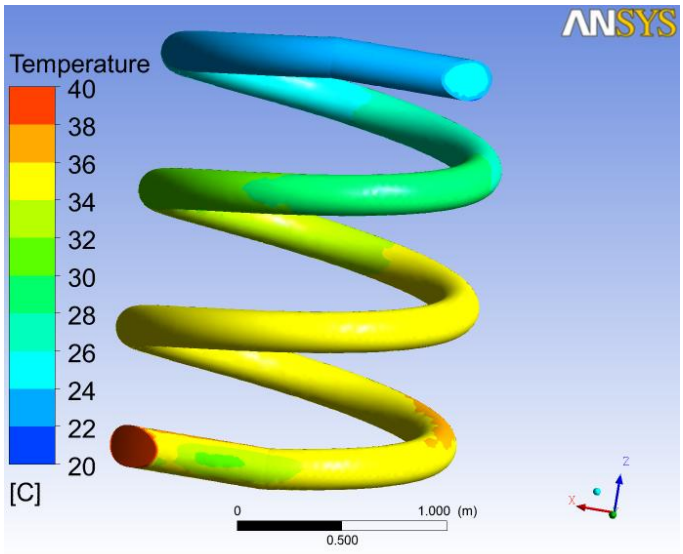

Figure 9. Three coils and hot fluid inlet temperature at 40°C – temperature map.

Study case 1: Inlet temperature of hot fluid at 25°C

Figure 8 show results for study case 1 with three coils, where the hot fluid inlet temperature is 25°C, for temperatures map. Figure 8 present homogeneity, a characteristic that was also observed for the heat exchanger with two coils. It was verified that a ΔT_{max} = 5°C is relatively significant, if the heat exchanger has two or three coils (Tables 6 and 7). The efficiency for the heat exchanger with three coils in the study case 1 was superior to the heat exchanger with two coils, so, in the case of small ΔT, the addition of a coil was significant.

Study case 2: Inlet temperature of hot fluid at 40°C

Figures 9 and 10 show results for study case 2 with three coils, where the hot fluid inlet temperature is 40°C, for

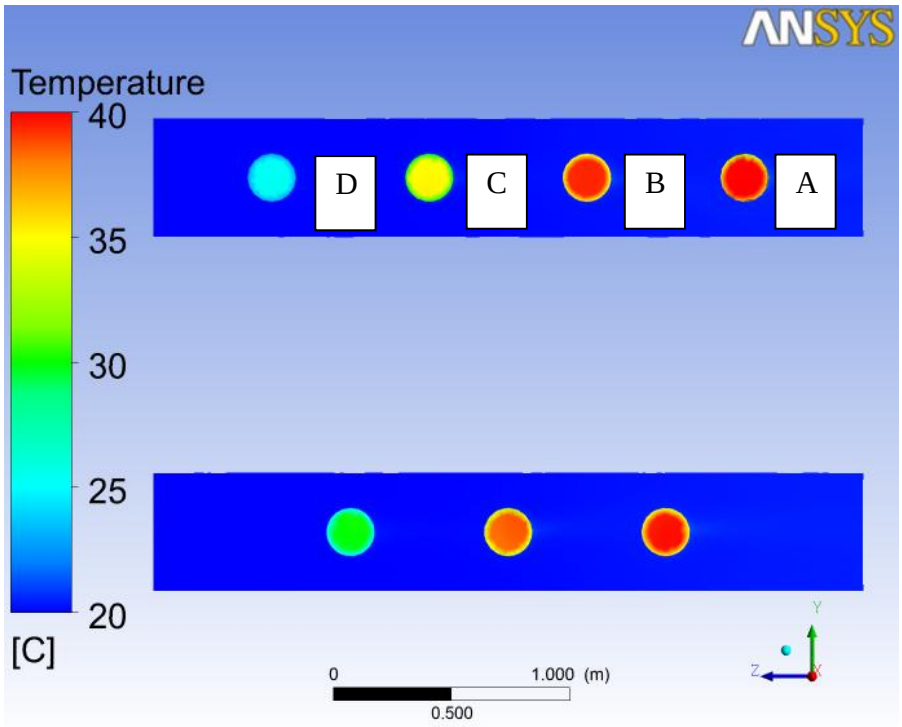

Figure 10. Three coils and hot fluid inlet temperature at 40°C – temperature.

temperatures diagram. Figures 9 and 10 show temperatures in sections A, B, C, and D. At the points B and C, the centre pipe has a slightly higher temperature if compared to the end. This fact can be justified, because the helically coil heat exchangers generated a secondary flow in the pipe core direction, benefiting the heat exchange in the ends. At point D, it is possible to check a considerable drop of temperature compared to point A. In the heat exchanger with two coils, it was not possible to see this significant difference between points A and D.

Table 7 presents the results for this simulation with an average efficiency. The efficiency for the heat exchanger with three coils in the study case 2 was superior to the heat exchanger with two coils. This fact is quite reasonable to be expected due to the greater area of heat exchanger than is achieved with one additional coil. It was also verified that for small ΔT, the difference about the efficiency is not significant.

Heat exchanger with simulations in other operating conditions

Figure 11 shows results for study case 1 with two coils and case 2 with three coils, where the hot fluid inlet temperature is 25 and 40°C, respectively for hot fluid inlet temperature, with simulations in other operating conditions (30°C and 35°C). When the hot fluid inlet temperature increases there seems to be an increase of the efficiency played by a secondary flow in the pipe core direction, for both cases. Figure 11 indicates a stronger effect of secondary flow as the temperature increases.

Conclusions

It can be concluded from this work that the difference in performance of the heat exchanger with two and three coils for a heat exchange relatively low, ΔTmax = 5°C between the refrigerant and fluid to be cooled, is very small, with no evident advantages for the heat exchanger with a larger number of coils. However, there was greater ΔT in study case 2, for example, ΔTmax = 30°C between refrigerant and fluid to be chilled. The performance efficiency of the heat exchanger with three coils compared to two coils showed considerably better efficiency. For the study case 2, with two coils, it was verified that the heat exchange efficiency was below that for the study case 1. It can be explained by the hot fluid inlet temperature to be higher in the study case 2 and the lower number of coils (two in this case).

It was not possible to perform suitable heat exchange, due to the smaller area of heat exchange and the inlet with higher temperature. This situation was not noticed in the heat exchanger with three coils. This research also revealed that it is necessary for future works to study the number of coils vs. project cost vs. heat exchanger performance for best optimization of the process of heat

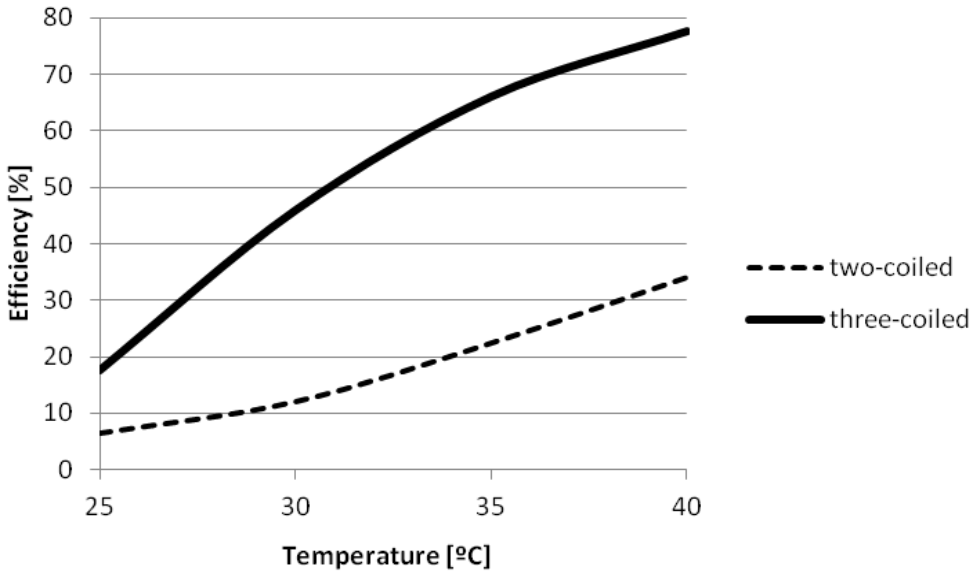

Figure 11. Efficiency-Temperature relationship of the heat exchanger with two and three coils.

exchange, due to the constant industrial need to reduction costs and work with best performances.

Conflict of Interests

The author(s) have not declared any conflict of interests.

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Scientific Research and Essays

Full Length Research Paper

Comparative study of protective effect of separate administration of vitamin C and folic acid in act therapy induced hepatic injury

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Artemisinin and its derivatives are among the most effective antimalarial drugs used today. This study compared the effects of pre-treatment with vitamin C and folic acid on the hepatotoxic effect of artemisinin combination. Thirty male wistar rats randomly assigned to six groups of five rats each were used in the study. Group A was the normal control; groups B, C, D, E and F were placed on therapeutic doses of leonart, leonart+vitamin C, leonart + folic acid, vitamin C and folic acid respectively. They were pretreated with the respective supplements for 28 days while administration of leonart was carried out for four days starting from the 24th day of supplements administration. The rats were thereafter sacrificed by cervical dislocation after an overnight fasting. Serum prepared from the whole blood and homogenized liver were then used for analysis. The result indicates that leonart administration raised the level of malaondialdehyde, serum total, conjugated bilirubin and the activities of alanine transaminase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP). It however decreases the activities of liver catalase, superoxide dismutase (SOD) and glutathione (GSH) level. Combined administration of leonart with vitamin C restored these parameters to pretreatment levels. Neither separate nor combined administration of folic acid with leonart altered any of these parameters.

Key words: Leonart, hepatotoxicity, artemisinin, antimalarial, oxidative stress.

INTRODUCTION

Malaria is considered to be a major public health problem in Nigeria. It causes more than 50% of the disease burden (Federal MoH, 2005) and almost 50% of all-cause health expenditure (Onwujekwe, et al., 2000). 20% of all hospital admissions, 30% of outpatient visits, and 10% of hospital deaths are attributable to malaria, and half of Nigeria's population is exposed to at least one episode of malaria every year (Okeke et al., 2006). Results of a

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modelling exercise presented in the National Malaria Control Program (NMCP) strategic plan 2009-2013 show that malaria accounts for an estimated 300,000 deaths in children under five each year and 11% of the maternal mortality burden in Nigeria. Malaria is responsible for 25% of all infant-related mortality and 30% of child-related mortality (ACT watch, 2009). In relative terms, Nigeria contributes more than a third of the total African malaria burden (RBM, 2008).

Malaria is a mosquito-borne infectious disease of humans and other animals caused by *Plasmodia* and are also definitely the single most destructive and dangerous infectious agent and the most serious health challenge in the developing countries of the world (Christopher et al., 2012). There were estimated 225 million cases of malaria worldwide in 2009. In 2010, there were 219 million malaria cases leading to approximately 660,000 malaria deaths, mostly among African children (UNICEF 2013).

Currently, artemisinin-based combination therapy (ACT) is recommended for the treatment of *P. falciparum* malaria (Singh et al., 2004; WHO, 2011). In the treatment, fast acting artemisinin based compounds are combined with a drug from a different class. The artemisinin-derivatives, artemether, artesunate, and dihydroartemisinin, are currently the most potent anti-malarial medicines on the market. They are widely available in the different pharmaceutical dosage forms including tablets, injections, suppositories and dry powders. Leonart (an artemeter-lumefantrine) was introduced as alternative drugs for the treatment of malaria in Africa due to the emergence of drug-resistant *Plasmodium falciparum*. The drug is effective in the treatment of malaria and, in artemisinin-based combination chemotherapy with other effective blood schinzonticide to prevent recrudescence and delay the selection of resistant strains. However, it is not recommended for the treatment of malaria caused by *Plasmodium vivax, Plasmodium ovale* and *Plasmodium malariae*, because other effective antimalarials are available. It is a fixed-dose combination of artemether and lumefantrine. It is used in the treatment of uncomplicated malaria caused by pure or mixed *P. falciparum* infections including strains from multidrug resistant areas and can prevent recrudescence after artemether therapy. Previous studies had reported that oral administration of artemisini-lumefantrine combination increases liver oxidative stress and caused significant elevation of serum alanine transaminase (ALT) and aspartate aminotransferase (AST) (Adaramoye et al., 2008).

Although medical doctors now prescribe the highly effective Artemisinin-based Combination Therapies (ACT) for the treatment of malaria, some study has however warned that taking ACT in combination with multivitamins that contain iron and vitamin C and E renders the drug ineffective (Looareesuwan et al., 1998; Patricia et al., 2009; Adumanya et al., 2012). The most prominent role of vitamin C is its immune stimulating effect, which is important for the defense against infections such as common colds. It also acts as an inhibitor of histamine, a compound that is released during allergic reactions. As a powerful antioxidant, it can neutralize harmful free radicals and aids in neutralizing pollutants and toxins. It is also able to regenerate other antioxidants such as vitamin E. Thus it is able to prevent the formation of potentially carcinogenic nitrosamines in the stomach (due to consumption of nitrite-containing foods, such as smoked meat) (Adunmaya et al., 2012). It has been reported that the concomitant administration of Artemisinin in various forms (Artemether, Arteether, Artesunate, Artenilate) with vitamin C and multivitamins - especially those preparations containing trace elements and minerals (such as Zinc, Copper, Iron (Fe^{2+}), etc) with antioxidant properties reduces the efficacy of the Artemisinin-based antimalarial drug therapy (George and Nmoka, 2003). However, there is paucity of information regarding the role of this vitamin in hepatic injury associated with ACT therapy. It is therefore, the purpose of this work to examine the protective role of vitamins C and folic acid on artemisinin-lumefantrine induced hepatotoxicity in rats.

MATERIALS AND METHODS

Drug

Leonart® composed of 80 mg Artemether and 480 mg lumefantrine was manufactured by Bliss GVS Pharma Ltd. India. And obtained from Fontana Pharmacy, Ijebu-Ode, Ogun State, Nigeria.

Experimental design

Thirty male adult rats of the Wistar Kyoto strain weighing 100 to 120 g obtained from the Animal house of the Department of Physiology, University of Ibadan, Nigeria were used for the study. All the animals were housed in metallic cages and maintained in well ventilated room provided with 12:12 h light and dark cycle for each 24 h period at a temperature of approximately 25°C. They were fed on pellets and tap water ad libitum. After the initial period of 7 days acclimatization, the animals were randomly assigned into 6 groups of 5 rats per group labeled as:

Group A (Normal control): Administered with normal saline
Group B (Test control 1): Administered with leonart
Group C (Test 1): Pre-treated with vitamin C thrice daily for 24 days and then administered with ACT combination therapy.
Group D: (Test 2): Pre-treated with folic acid for 24 days and then administered with leonart combination therapy.
Group E (Test control 2): Administered with vitamin C.
Group F (Test control 3): Administered with folic acid.

Drug administration

Leonart was administered at a therapeutic dose of 2.67 mg artemether/16 mg lumefantrine per Kg body weight twice daily. Vitamin C was administered at a dose of 53.71 mg/kg thrice daily

Table 1. Effect of pre-treatment with vitamin C and folic acid on leonart induced oxidative stress.

Group/Treatment	MDA (µmol/mg)	Catalase activity µmol/mg protein	SOD activity µmol/mg protein	GSH (µg/g tissue) x10^3
Group A (Normal saline)	1.49 ± 0.04^a	170.33±1.56^a	0.55±0.40^a	17.02±0.05^a
Group B: (Leonart)	2.14±0.10^c	161.67±2.63^c	0.42±0.35a	12.14±0.03^c
Group C (Leonart + Vitamin C)	1.51 ± 0.07^a	196.67±1.8	0.72±0.24^a	15.63±0.51^a
Group D (Leonart + folic acid)	1.66±0.06^b	87.24±6.91^c	0.58± 0.06^a	16.01±0.05^a
Group E (Vitamin C)	1.41 ± 0.04^a	159.67±6.06^a	0.63±0.43^a	16.09±0.06^a
Group F (Folic acid)	1.46 ±0.02^a	149.04± 8.61^a	0.67± 0.05^a	16.61±0.12^a

Results are mean ± SEM of 5 determinations, values in the same column with similar superscripts are not significantly different from each other.

while folic acid was administered at a dose of 50 mg/kg. Groups C, D, E and F were treated with the respective supplement for 28 days. On the 24th day after the commencement of treatment, leonart administration was carried out in the rat groups B, C and D. The administration was done for the next four days at the respective dosage.

Preparation of tissue homogenate

Rats were sacrificed 24 h after the last administration of leonart and or supplements after an overnight fast. Liver were quickly removed and washed in ice-cold 1.15% KCl solution, dried and weighed. The liver samples were homogenized in 4 volumes of 5 mM phosphate buffer, pH 7.4 and centrifuged at 10,000 ×g for 15 min to obtain post-mitochondrial supernatant fraction. The samples were stored at –80°C until use. All procedures were carried out at temperature 0 to 4°C.

Preparation of serum

Blood was collected from the inferior *vena cava* of heart of the animals into plain centrifuge tubes and was allowed to stand for 1 h. Serum was prepared by centrifugation at 3000 × g for 15 min in a centrifuge. The clear supernatant was used for analysis.

Assay procedure

Protein determination

Serum and liver protein levels were determined according to the method of Lowry et al. (1951), using bovine serum albumin as standard.

Total and conjugated bilirubin concentration

The bilirubin levels (total and direct) were assayed for by the method of Rutkowski and Debaare (1966). The method is based on the reaction between bilirubin and diazotized sulfanilic acid in alkaline medium to form a blue-coloured complex, which was read spectrophotometrically at 546 nm.

Liver dysfunction marker enzymes

Serum alanine aminotransferase (ALT) and aspartate aminotransferases (AST) activities were determined using a combination of the methods of Mohun and Cook (1957), and Reitman and Frankel (1957). The estimation of alkaline phosphatase (ALP) activities was based on the method of Williamson (1972). ALP activity was measured spectrophotometrically by monitoring the concentration of *p*-nitrophenol formed when ALP reacts with *p*-nitrophenyl phosphate at 405 nm.

Liver oxidative stress

The extent of lipid peroxidation (LPO) was estimated by the method of Buege and Aust (1978). The method involved the reaction between malondialdehyde (MDA; product of LPO) and thiobarbituric acid to form a pink precipitate, which was read at 535 nm spectrophotometrically. Superoxide dismutase (SOD) activity was measured by the nitroblue tetrazolium reduction method of McCord and Fridovich (1969); Catalase (CAT) activity was assayed by measuring the rate of decomposition of hydrogen peroxide at 240 nm as described by Aebi (1974); reduced GSH level was assayed by measuring the rate of formation of chromphoric product in a reaction between DTNB (5,5′-dithio-bis (2-nitrobenzoic acid) and free sulfhydryl groups (such as reduced glutathione) at 412 nm according to the method of Moron et al. (1979).

Statistical analysis

All values were expressed as mean ± S.D. The statistical analysis was carried out using one-way analysis of variance (ANOVA) followed by Duncan's Multiple Range Test (DMRT) (Duncan, 1957). Test with $P< 0.05$ were considered significantly different.

RESULTS

Leonart was observed in the study to increase the MDA value significantly above the normal control value and also reduced the catalase activity but does not significantly altered the liver SOD activity significantly (Table 1). Combined administration of vitamin C and leonart lowers the level of peroxidation to pretreatment value and also increased the catalase activity above the normal control level but does not significantly altered the SOD activity. Table 1 also indicates that whereas separate administration of folic acid neither altered the liver MDA level nor the antioxidant enzyme activities, its combined administration with leonart raised the level of peroxidation above the normal control value (though the value obtained was lower than that which was observed

Table 2. Effect of combined administration of supplements and leonart on some liver enzymes.

Group/Treatment	Liver enzyme activity (U/L)		
Group/ Treatment	**ALP**	**ALT**	**AST**
Group A (Normal saline)	84.57±12.85[a]	24.33±1.23[a]	52.33±8.69[a]
Group B: (Leonart)	143.00±1.84[c]	36.00±2.89[b]	71.83±1.78[c]
Group C (Leonart + vitamin C)	106.67±4.21[b]	25.66±1.74[a]	66.17±2.22[b]
Group D (Leonart + folic acid)	113.85±2.59[b]	30.00 5.07[a]	52.00 3.14[a]
Group D (Vitamin C)	91.65±2.48[a]	20.17±1.34[a]	44.00±1.06[a]
Group F (folic acid)	81.75± 2.45[a]	20.03± 1.84[a]	55.00± 3.18[a]

Results are mean ± SEM of 5 determinations, values in the same column with similar superscripts are not significantly different from each other.

Table 3. Effect of combined administration of supplements and leonart on serum bilirubin and total protein.

Group/ Treatment	Total bilirubin (mg/dL)	Conjugated bilirubin (mg/dL)	Total protein (mg/dL)
Group A (Normal saline)	4.60±0.06[a]	3.00±0.05[a]	105.10±5.63[a]
Group B: (Leonart)	7.60±0.07[c]	4.30±0.01[b]	90.08±5.77[b]
Group C (Leonart + vitamin C)	4.80±0.04[a]	3.02±0.03[a]	100.06±5.92[a]
Group D (Leonart + folic acid)	6.89±0.13[b]	4.10±0.01[b]	112.11±3.18[a]
Group E (Vitamin C)	4.00±0.06[a]	3.20±0.04[a]	102.06±3.16[a]
Group F (folic acid)	4.00±0.06[a]	3.10±0.05[a]	105.24±3.12[a]

Results are mean ± SEM of 5 determinations, values in the same column with similar superscripts are not significantly different from each other.

when leonart was administered alone). No significant alteration was found in the liver catalase and SOD activities when folic acid was administered separately (when compared with that of the normal control). Combined administration of leonart and folic acid however significantly lowered the liver catalase activity. The observed activity was also lowered than that of the normal control value and that obtained with vitamin C administration and when vitamin C was combined with leonart. The result of the liver GSH analysis also indicates that leonart administration significantly reduced the liver GSH below the normal control value. When leonart was co-administered with vitamin C, the liver GSH was brought to the pre treatment level. Neither separate treatment with folic acid and vitamin C nor combined administration of folic acid with leonart was observed to have altered the liver GSH level.

The result also shows that separate administration of leonart increased the serum ALP, ALT and AST activities above the normal control values. When leonart administration was combined with vitamin C, the serum ALP and AST activities were significantly reduced below that obtained with separate administration of leonart but the observed activities were also higher than the normal control values. The liver enzyme activities were not significantly altered with separate administration of folic acid. The ALP activity was however raised above the normal control value when folic acid administration was combined with leonart. When the enzyme activities were compared when folic acid and vitamin C were separately administered, they were not observed in this study to be significantly different (Table 2).

Result of the serum bilirubin shown in Table 3 indicates that administration of leonart significantly raised serum total and conjugated bilirubin significantly above the normal control values. When leonart was co-administered with vitamin C, the observed total and conjugated bilirubin values were not different from that of the normal control values. Co-administration of leonart and folic acid however raised the total and conjugated bilirubin level above the normal control values. The observed values were also higher than that obtained when folic acid was separately administered. The table also indicates that leonart administration significantly lowered serum total protein level below the normal control value. The serum total protein however does not vary significantly when leonart was co-administered with either vitamin C or folic acid neither was it altered with separate administration of vitamin C and folic acid.

DISCUSSION

The increased oxidative stress observed in this study which is evident with increased liver MDA level and reduced liver antioxidant status with leonart administration is a confirmation of previous reports on the oxidative stress associated with artemisinin combination

therapy (Adaramoye et al., 2008; Paul et al., 2010; Akomolafe et al., 2011). The significant increase in MDA concentration observed in leonart administered rats is an indication of the tendencies of leonart to predispose to oxidative stress. Artemisinin in its chemical structure contains a fragile di-oxygen (O---O) bridge and its antiplasmodial action is predicated on the generation of an oxygen centered free radical due to transient cleavage of this bridge which thus results in lipoprotein oxidation, endothelial dysfunction and vascular damaging. The uptake of oxidized LDL particles by scavenger receptors present in macrophages triggers a series of events, leading to production of foam cells and therefore the formation of atherosclerotic plaque (Nwanjo et al., 2007). Vitamin C has been shown in our study to reduce the oxidative stress induced by leonart administration. This is evident by the reduction in liver MDA and increased liver GSH and catalase activity when vitamin C was co-administered with leonart. The mechanism by which this was achieved may be due to the antioxidant property of vitamin C. Vitamin C, being antioxidant will mop up free radical generated by the transient cleavage of the endoperoxide bridge in the artemisinin structure thereby reducing the level of liver peroxidation. It may however, also be important to point out here that the antimalarial activity of leonart is a function of the oxidation effect of the drug. An antioxidant such as vitamin C therefore that does mop up the free radicals when co-administered with artemisinin combination drug such as leonart, although may be beneficial in reducing liver oxidative stress (as evident in our study) but may also incapacitate the drug molecule and may reduce the effectiveness of its anti protozoal action as it may increase plasma concentrations of the drug and delays reaching peak drug concentration (Owira and Ojewole, 2010). This may thus increase the risk of serious malarial problems.

Folic acid administration in this study was not seeing to have either reduce or increase the level of oxidative stress that was associated with leonart administration. Folic acid (folate) is a water-soluble B-vitamin whose biologically active form is tetrahydrofolic acid (THF), which participates in the transfer of 1-carbon units (such as methyl, methylene, and formyl groups) to the essential substrates involved in the synthesis of DNA, RNA, and proteins (Bailey and Gregory, 1999). Ingested folic acid can be converted to its physiological forms. This process is initiated by dihydrofolate reductase in a two-step reaction; the first step being the conversion to dihydrofolate (DHF). This is a slow and rate-limiting step (Wagner, 1995). In the second, more rapid step, dihydrofolate is further reduced to THF. THF can then be converted into additional physiological folates including 5-methyl-THF, the form that is found in circulation and in tissues (Parcia et al., 2008). Folic acid especially at high doses has been reported to counteract the efficacy of antimalarial drug sulfadoxine-pyrimethamine (UNICEF, 2013). Our study does not suggest a similar effect with leonart.

The liver plays a central role in transforming and clearing chemicals and is susceptible to toxicity from these agents. This is primarily because of its unique metabolic responsibility and close relationship with the GIT. Consequently, certain medicinal agents when taken in overdose and sometimes even when introduced in therapeutic ranges may injure the organ. Liver enzymes are usually raised in acute hepatotoxicity, but tend to decrease with prolonged intoxication due to damage to the liver (Obi et al., 2004). Previous studies have reported that some antimalarial agents such as chloroquine (Pari and Amali, 2005) and amodiaquine (Farombi et al., 2000) can induce hepatic damage. The pharmacokinetics of ACTs shows that their primary site of metabolism is the liver, thus it would be expected that the liver would be susceptible to injury from these agents. Previous authors however, did not agree on the capacity of ACT to induce liver injuries. Whereas Adaramoye et al. (2008) reported increased liver damage in rats administered with ACT, Georgewill and Ebong (2012) reported a normal hepatic cells in mice administered with ACT. In the present study, we observed increased serum ALT, ALP and AST activities in rats treated with therapeutic dose of leonart. This may suggest the ability of the drug to predispose to hepatic injury. Furthermore, our study indicates that co-administration of vitamin C with artemisinin may prevent this hepatic injury predisposition. Bilirubin is a tetrapyrrole created by the normal breakdown of heme. Most bilirubin is produced during the breakdown of hemoglobin and other hemoproteins. Accumulation of bilirubin or its conjugates in body tissues produces jaundice which is characterized by high plasma bilirubin levels and deposition of yellow bilirubin pigments in skin, sclerae, mucous membranes, and other less visible tissues (Tiribeli, 2005; Drummond and Kappas, 2004). An elevated level of bilirubin in the blood may indicate liver disease or drug-induced liver damage. Elevations of direct bilirubin typically result from obstruction either within the liver (intrahepatic) or a source outside the liver (e.g. gallstones or a tumor blocking the bile ducts). Bilirubin measurements are especially valuable in newborns, as extremely elevated levels of unconjugated bilirubin can accumulate in the brain, causing irreparable damage.

The result of alteration in both total and conjugated bilirubin level in leonart administered rats' correlates with that of variation in liver enzymes which also suggest the ability of the therapeutic administration of the drug to induce liver injury and the efficacy of vitamin C to prevent this damage. The study thus suggests that the vitamin offer protection by preserving the structural integrity of hepatocellular membrane against ACT injury. The ability of the vitamin to offer this protection could also be attributed to its antioxidative effect which was also confirmed in our study. This finding correlates with previous study, which reported that treatment with

tetrahydrocurcumin (an antioxidative substance derived from curcumin, the component of turmeric) significantly reduced the activities of serum hepatoxicity markers in chloroquine-induced hepatoxicity (Pari and Amali, 2005) and erythromycin-induced hepatoxicity (Pari, 2004). We however do not observe the same protection with folic acid administration.

Conclusion

The result of our study correlates' with previous findings that therapeutic dose of artemisinin combination therapy may induce hepatotoxicity. This study also indicates that co-administration of ACT with vitamin C may offer hepatotoxic protection but that co-administration of the drug with folic acid may not. We however, suggest caution in administering vitamin C along with ACT since the antioxidant activities of the vitamin may mop up the free radicals generated by the cleavage of the di oxygen bridge of the drug and this may reduce the efficacy of the drug against the malarial plasmodium.

Conflict of Interests

The author(s) have not declared any conflict of interests.

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Scientific Research and Essays

Full Length Research Paper

Estimation of number of generations of *Spodoptera litura* Fab. on peanut in India during near and distant future climate change scenarios

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Studies were conducted to estimate the impact of increase in temperature on number of generations of tobacco caterpillar, *Spodoptera litura* on peanut for seven different locations of various agro ecological zones of the country for baseline (1961 to 1990), present (1991 to 2005), near future (2021 to 2050) and distant future (2071 to 2098) climate change (A1B) scenarios. The daily minimum and maximum temperature (MinT and MaxT) records were used to obtain cumulative degree days (DD) for each generation of insect using a temperature threshold of 10°C. Faster accumulation of degree days will making it possible for one or two additional generations with shortened life cycle (completion of generation would be 5 to 6 days earlier) of *S. litura* was inferred for both near and distant-future climate change scenarios (CCS) compared to baseline and present periods, at all locations. The additional number of generations and variation in the generation time of *S. litura* across seven growing locations of India imply the definitive and differential impacts, respectively of the projected increasing temperature in the future CCS.

Key words: *Arachis hypogaea*, climate change scenario, degree days, generation time, number of generation, *Spodoptera litura.*

INTRODUCTION

During this century, global mean temperature has been predicted to rise by 2 to 5°C. Climate model projections were summarized in the 2007 Fourth Assessment Report (AR4) by the Intergovernmental Panel on Climate Change (IPCC). They indicated that during the 21st century the global surface temperature is likely to rise a further 1.1 to 2.9°C (2 to 5.2°F) for their lowest emissions scenario and 2.4 to 6.4°C (4.3 to 11.5°F) for their highest (IPCC, 2007). Though climate change is global in its occurrence and consequences, it is the developing countries like India that face more adverse impacts as majority of the population depends on agriculture with excessive pressure on natural resources and because of poor coping mechanisms. Increasing temperatures and

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atmospheric CO_2 have been very significant during the last three decades (Stern, 2007) influencing all sectors of agriculture. Within agriculture, how the climate change impacts insect pests and diseases is an important area that is engaging biological scientists. Climate change projections made up to 2100 for India indicate an overall increase in temperature by 2 to 4°C with no substantial change in precipitation quantity (Krishna Kumar, 2011). Last three decades witnessed a sharp rise in mean annual temperature in India (Venkateswarlu, 2009).

Analysis of data for the period 1901 to 2005 by Indian Meteorological Department (IMD) suggested that annual mean temperature for the country as a whole increased by 0.51°C over the period. It may be mentioned that annual mean temperature has been consistently above normal (base period: 1961 to 1990) since 1993. This warming is primarily due to rise in maximum temperature over a larger part across the country.

Peanut (*Arachis hypogaea* L.) also known as groundnut, earthnut and ground bean, is the world's fourth most important source of edible vegetable oil and third most important source of vegetable protein. Production is concentrated in Asia (50% of global area and 64% of global production) and Africa (46% of global area and 28% of global production), where the crop is grown mostly by smallholder farmers under rainfed conditions with limited inputs. China, India, Nigeria, USA and Myanmar are the major peanut growing countries. India is the second largest producer of peanut in the world with an average annual production of 5.51 million tons (http://faostat.fao.org) from an area of 5.47 million ha. Productivity levels of peanut in India is1007 kg/ha as against 1522 kg/ha of the globe and 3356 kg/ha of China. Elevated CO_2 was reported to cause significant increase in total biomass at final harvest of peanut crop but decreased final seed yield in selected cultivars (Bannayan et al., 2009). The tobacco caterpillar, *Spodoptera litura* (Fab.) is a major pest which can cause yield losses of 35 to 55% and larvae feed gregariously on leaves causing severe defoliation, leaving only midrib veins. Insects are physiologically sensitive to temperature, have short life cycle and great mobility, and their developmental rate and geographical distribution are therefore highly responsive to changes in temperature (Lange et al., 2006). Insect developmental rate, geographical distribution and the intensity of their feeding increased historically with increasing temperature (Bale et al., 2002) and resulting in increased herbivory and insect diversity. The increase in surface temperatures would permit multivoltine species to increase the number of generations per year or during crop season. It is well known that the relationship between climate change and voltinism could be more complex. The number of generations is used as a parameter to assess the role of temperature on population dynamics of the insect pest.

The present study is aimed to estimate and quantify the impact of increase in temperature on number of generations of *S. litura* on peanut crop considering four different climatic periods *viz*; baseline, BL (1961 to 1990), present, PR (1991 to 2005), near future, NF (2021 to 2050) and distant future, DF (2071 to 2098) for seven major peanut growing locations of the country.

MATERIALS AND METHODS

The work comprises of three components *viz;* (i) obtaining historical data and climate projections on daily temperature from respective grid points, (ii) computation of growing degree days (GDD) for completion of life cycle of *S. litura* based on the threshold temperature and (iii) estimation of the possible number of generations during crop season in the future projected climate by substituting the projections on the temperature using SRES A1B scenario.

Collection of historical temperature data

Historical daily temperature (maximum and minimum) for seven study locations *viz*; Jalgaon (21° 5' N, 75° 40' E); Raichur (16° 12' N, 77° 25' E); Bhubaneswar (20° 16' N, 85° 50' E); Hayathnagar (17° 18' N, 78° 60' E); Tirupathi (13° N, 79° E); Jagityal (18° 8' N, 78° 9' E); and Kadiri (14° 12' N, 78° 10' E) were collected from a 1x1 degree grid database provided by IMD (Srivastava et al., 2008) for the period 1991 to 2005 being referred as a present (PR) period in this research.

Estimation of number of generations of *S. litura* on peanut

The standard GDD approach was followed to estimate the number of generations of *S. litura* occurring on peanut during a crop season. The maximum and minimum temperatures were transformed to heat units using the lower threshold temperature of (t_0) 10°C for *S. litura* on peanut and the standard method for estimation of the degree days (Thermal requirements) for each day was calculated by using the formula (Elsaadany et al., 2000).

$H = \Sigma$ D-D

Where:

H=Number of heat unit to emergence.

D-D = (Max. t. + Min. t.)/2 – t_0, if Max. t.>t_0<Mint

t_0= threshold temperature = 10°C.

The minimum and maximum daily temperatures of different periods (BL, NF and DF) were used for estimating the accumulated thermal heat units. The degree days required for completing life cycle of *S. litura* (egg to adult) on peanut was taken as 522.7 DD (Ranga Rao and Wightman, 1989) and GT generation time (average development time) needed for completion of one cycle was estimated. The number of generations of *S. litura* was calculated using cumulative degree days (Degree Day Units) for each generation of insect. Web introduction for the Insect Development Database (IDD) was consulted for obtaining the degree day units of these insect pests (www.nappfast.org/databases/). The website has database on thermal requirements of several insect pests, which is maintained by The North Carolina State University-APHIS Plant insects' life cycle esp. number of generations during the season by

Pest Forecast (NAPPFAST) System and Global Pest and Disease Database (GPDD). GDD approach can be used to predict the measuring the growth in terms of temperature over time and considers average daily temperatures which influence insect development.

Expected number of generations were estimated using INGEN (β – version) software developed at CRIDA, wherein accumulated thermal degree days was calculated by horizontal cut-off (degree-day accumulations above the upper threshold do not count) method. The software provides data on GT (Generation Time) in days as given above, Mean GDD (Mean Growing Degree Days - accumulated degree days to complete one generation after reaching cut-off GDD) and Total Degree Days (TDD - total summation of the degree days in a calendar year or crop season).

Future climate data

A number of global circulation models with their corresponding versions of downscaled projections at a relatively smaller spatial resolution are available and the projections vary from the parent GCM (Krishna Kumar et al., 2011). In this paper, we utilize the projections obtained at a resolution of 50 × 50 km grid using the PRECIS where the daily data on maximum temperature, minimum temperature and rainfall are available for the period between 1961 and 2098. The output for the A1B emission scenario showing 'reasonable skill in simulating the monsoon climate over India' (Krishna Kumar et al., 2011) was considered. A1B is 'the most appropriate scenario as it represents high technological development, with the infusion of renewable energy technologies following a sustainable growth trajectory' (MoEF, 2012). The future temperature data thus obtained were classified into two categories *viz*; 'near future' (NF) consisting of 2021 to 2050 and distant future (DF) consisting of 2071 to 2098. The period between 1961 and 1990 was referred as the base line (BL) period.

Accumulation of degree days was calculated considering the specific biological event called as "biofix". In this case the pheromone trap 'first catch' was considered as a Biofix and the cumulative degree days for *S. litura* was estimated for the crop season covering 133 days of crop duration across seven locations. The analysis of historical data on pheromone trap catch across various locations was reported by following the first order Markov chain probability model (Victor et al., 2003). A first order Markov chain probability model was adopted to estimate the probabilities of occurrence of pheromone trap catch which was > 30 adult moths / week. The results indicated that the probability of occurrence of pheromone trap catch was significant during the entire crop season ranging from 26 to 44 standard week (swk) comprising 133 days of crop duration mostly (Srinivasa Rao et al., 2012).

Statistical analysis

The data on variation in number of generations of *S. litura* across seven locations for the four periods *viz;* base, present, near and future periods were analyzed using the Kendall Family of Trends test (Helsel et al., 2006). The mean number of generations in BL, PR, NF and DF scenarios was compared using two-sample t-test assuming equal variances. The significance of mean values was defined at $p< 0.01$ and all statistical analysis were done using SPSS version 16.0.

RESULTS AND DISCUSSION

The findings on the possible number of generations during peanut crop season, time taken to complete a generation and the inter-generation variations therein are presented hereunder.

Variation in total accumulated degree days (TDD) and number of generations

Results on the variation in accumulated degree days of *S. litura* at seven peanut growing locations are presented in Table 1. The insect *S. litura* accumulated lower thermal degree days of 2193 and higher of 2493 DD at Jalgaon and Tirupathi during the present period accommodating about 4.20 and 4.77 generations respectively (Table 2). The mean growing degree days of the insect was in the range of 522.7 DD as the units are universal and will not vary with the locations. The number of degree days increased to 2393 DD during near-future and 2689 DD during the distant-future making it possible to complete one more generation compared to the current climatic conditions at Jalgaon. At Kadiri, the number of generations possible increased to between five and six (4.89 to 5.50) during near and distant future climate scenarios resulting in two generations higher than current climatic periods. In other locations also, it is predicted that the higher accumulation of degree days would be possible during both the near and distant-future climate change scenarios (CCS) and expected to accommodate one or two additional generation during the crop season compared to four generations during the base line and present periods.

The mean number of generations among four climate scenarios analyzed using t-test indicated that the variation was significant at majority of locations. Increased number of generations are expected during NF ($p=< 0.01$; $t= 5.05$) and DF ($p=< 0.01$; $t= 11.78$) scenarios at Raichur and NF ($p=< 0.01$; $t= 8.06$) and DF ($p=< 0.01$; $t= 12.74$) Jalgaon, during NF ($p=< 0.01$; $t= 8.96$) and DF ($p=< 0.01$; $t= 19.90$) Bhubaneswar locations. The expected number of generations would be higher by one and the increased number of generations were predicted to be significant in NF scenario at Kadiri ($p=< 0.01$; $t= 7.48$). The predicted number of generations would vary significantly in NF scenario at Tirupathi ($p=< 0.01$; $t= 0.71$) and at Jagityal NF ($p=< 0.01$; $t= 0.84$). In rest of locations the increase in number of generations was found to be highly significant during NF over present climatic conditions (Table 2). It was expected that there would be significant increase in number of generations at all peanut growing locations during DF scenario.

The percent change in the variation of number of generations of *S. litura* under present and future climate change-NF and DF scenarios over BL period at four locations indicated that the percent increase was found to be minimum (0 to 5%) during the present period however, the increase was higher (19 to 27%) DF and (8 to 13%) NF scenarios over BL period.

Table 1. Mean generation time (GT) and total accumulated degree days (TDD) of *S. litura* on peanut under climate change scenario (CCS).

Name of the location	Current climate period					
	Base Line			Present		
	Mean GT	Mean GDD	TDD	Mean GT	Mean GDD	TDD
Jalgaon	31.71± 0.42	526.04 ±3.23	2223.35 ± 119.07	31.73 ±1.23	525.66 ±7.30	2193.58 ± 56.86
Raichur	32.41 ± 1.85	524.62 ± 2.61	2138.00 ± 128.12	30.76 ± 0.73	524.61 ± 4.09	2251.71 ± 38.81
Kadiri	29.94 ± 0.47	524.98 ± 4.37	2315.67 ± 94.79	29.10 ± 0.89	524.84 ± 6.38	2366.84 ± 49.04
Bhubaneswar	29.18 ± 0.54	524.77 ± 5.11	2351.20 ± 41.17	29.35 ± 0.27	524.84 ± 4.80	2347.63 ± 52.32
Tirupathi	30.08 ± 1.36	524.36 ± 5.73	2280.39 ± 86.46	27.36 ± 0.83	525.08 ± 5.80	2493.59 ± 47.56
Hayathnagar	32.62 ± 0.99	524.66 ± 4.38	2101.05 ± 121.60	29.06 ± 0.84	524.42 ± 5.63	2371.72 ± 37.28
Jagityal	33.80 ± 2.57	523.14 ± 5.60	1994.94 ± 96.64	31.01 ± 0.77	524.90 ± 5.58	2234.71 ± 40.04

Name of the location	Climate change scenario					
	Near future			Distant future		
	Mean GT	Mean GDD	TDD	Mean GT	Mean GDD	TDD
Jalgaon	29.41 ± 0.98	525.08 ± 3.32	2393.23 ± 86.75	25.80 ± 2.54	524.87 ± 4.42	2689.09 ± 144.18
Raichur	28.29 ± 2.50	523.58 ± 4.59	2407.09 ± 115.37	25.53 ± 1.64	524.37 ± 4.87	2722.43 ± 140.61
Kadiri	26.93 ± 0.65	524.24 ± 4.55	2556.55 ± 92.29	24.13 ± 0.22	524.68 ± 5.01	2873.01 ± 103.56
Bhubaneswar	27.20 ± 0.38	523.40 ± 5.98	2534.18 ± 70.71	24.83 ± 0.72	524.58 ± 5.69	2800.50 ± 79.57
Tirupathi	27.39 ± 1.03	524.96 ± 4.11	2511.76 ± 91.39	24.38 ± 0.97	525.11 ± 5.23	2826.93 ± 99.56
Hayathnagar	30.29 ± 1.00	524.95 ± 4.34	2302.89 ± 102.44	26.11 ± 1.54	524.83 ± 5.24	2650.29 ± 127.47
Jagityal	32.04 ± 1.11	525.35 ± 4.83	2212.13 ± 91.84	26.85 ± 3.00	524.26 ± 4.98	2543.11 ± 135.76

Mean GT: Mean generation time, Mean GDD: Mean growing degree days, Mean TDD: Mean total degree days.

Table 2. Variation in number of generations (mean ± standard deviation) of *S. litura* across seven peanut growing locations.

Name of the location	Current climate period		Climate change scenario	
	Base line	Present	Near future	Distant future
Jalgaon	4.25 ± 0.23 (0.87) ^{NS}	4.20 ± 0.11	4.58 ± 0.17 (8.06)**	5.14 ± 0.28 (12.74)**
Raichur	4.09 ± 0.25 (3.34) **	4.31 ± 0.07	4.61 ± 0.22 (5.05)**	5.21 ± 0.27 (11.78)**
Kadiri	4.43 ± 0.18 (1.87)**	4.53 ± 0.09	4.89 ± 0.18 (7.48)**	5.50 ± 0.20 (17.85)**
Bhubaneswar	4.50 ± 0.08 (0.22) ^{NS}	4.49 ± 0.10	4.85 ± 0.14 (8.96)**	5.36 ± 0.15 (19.90)**
Tirupathi	4.36 ± 0.17 (8.86)**	4.77 ± 0.09	4.81 ± 0.17 (0.71) ^{NS}	5.41 ± 0.19 (12.19)**
Hayathnagar	4.02 ± 0.23 (8.32) **	4.54 ± 0.07	4.41 ± 0.20 (2.44)**	5.07 ± 0.24 (8.27)**
Jagityal	3.81 ± 0.18 (9.11) ^{NS}	4.28 ± 0.08	4.23 ± 0.18 (0.84) ^{NS}	4.87 ± 0.26 (8.60)**

Figures in parentheses are 't'- values, and BL, NF and DF were compared over PR. ** Indicate the statistical significance compared over present period at p<0.01 and NS: not significant.

Mann-Kendall test was performed to evaluate the trend in the number of generations of *S. litura* during the crop season under different climate change scenarios indicated a very high positive value of Mann-Kendall statistic (S), at Bhubaneswar denoting an increasing trend under the four climatic conditions being significant for NF (p= <0.01; tau C= 0.51) and DF (p= <0.01; tau C= 0.30) scenarios. Similar increasing trend during NF and DF climate change scenarios at all centers except at Jalgaon with non significant trend in NF scenario (p= 0.16 (>0.01); tau C= 0.18). Non significant temporal variation of *S. litura* was observed during BL and PR periods at Kadiri, Tirupathi and Hayathnagar, whereas, significant increasing trend was predicted to occur during NF (p= <0.01; tau C= 0.33, p= <0.01; tau C= 0.30 and p= <0.01; tau C= 0.37) and DF (p= <0.01; tau C= 0.34, p= <0.01; tau C= 0.30 and p= <0.01; tau C= 0.42) climatic scenarios. Overall, it is expected that there would be an increasing trend of number of generations (by one or two generations) during future climate change scenarios at majority of locations including Raichur and Jalgaon (Table 3) peanut growing centers.

Table 3. Temporal trends in number of generations of *S. litura* across seven peanut growing locations using Mann Kendall Test.

Name of the location	Climate scenario	No. of data points	Tau correlation co-efficient	Mann Kendall statistic (s)	Normalized test statistic (Z)	Probability	Trend
Jalgaon	**BL**	30	0.16	69	1.215	0.23	NS
	PR	15	-0.24	-25	-1.19	0.23	⬇
	NF	30	0.18	80	1.419	0.16	NS
	DF	28	0.29	112	2.199	0.03*	⬆
Raichur	**BL**	30	0.25	111	1.96	0.05*	⬆
	PR	15	0.12	13	0.59	0.55	NS
	NF	30	0.23	101	1.78	0.07*	⬆
	DF	28	0.29	112	2.19	0.03*	⬆
Kadiri	**BL**	30	0.18	77	1.36	0.17	NS
	PR	15	0.18	19	0.89	0.37	NS
	NF	30	0.33	142	2.52	0.012*	⬆
	DF	28	0.34	128	2.51	0.01*	⬆
Bhubaneswar	**BL**	30	0.25	111	1.96	0.05*	⬆
	PR	15	0.52	55	2.67	0.007*	⬆
	NF	30	0.51	221	3.96	0.0001*	⬆
	DF	28	0.301	115	2.25	0.02*	⬆
Tirupathi	**BL**	30	0.13	59	1.03	0.30	NS
	PR	15	0.31	33	1.58	0.11	NS
	NF	30	0.30	132	2.34	0.02*	⬆
	DF	28	0.30	114	2.23	0.02*	⬆
Hayathnagar	**BL**	30	0.20	87	1.53	0.13	NS
	PR	15	0.01	1	0.00	1.00	NS
	NF	30	0.37	163	2.89	0.004*	⬆
	DF	28	0.42	160	3.14	0.002*	⬆
Jagityal	**BL**	30	0.19	83	1.46	0.14	NS
	PR	15	-0.37	-39	-1.88	0.06*	⬇
	NF	30	0.40	175	3.10	0.002*	⬆
	DF	28	0.37	140	2.75	0.006*	⬆

BL- Base line, PR- Present, NF- Near future and DF- Distant future. *Significance at p<0.01 and NS- not significant. ⬆ Indicates increasing trend.

Mean number of generations and generation time

The increase in number of generations is obviously due to the reduction in the time taken to complete a generation for the insect made possible by the faster accumulation of required heat units. Variations in mean generation time of *S. litura* during different climate scenarios at four peanut growing locations which represents different states of the country are depicted in Figure 1. The average length of time taken to complete life cycle of *S. litura* at Jalgaon was found to be 29 and 26 days during the near and distant-future compared to 31 and 32 days during the BL and PR climatic periods, respectively. The similar reduction of generation time is evident across three generations also recorded. The first generation took longer time with 31 days during both BL and PR periods and was expected to complete 29 days in NF and 26 days in DF scenarios. Second and third generations were predicted to occur in shorter time than in BL and PR periods. The results of climate change scenario (DF) at same centre indicated one additional generation with a reduced life cycle of 25 days of the pest would be possible. At Raichur the generation time of *S. litura* was found to be 32 and 31 days in BL and PR periods and it is expected that life cycle of pest would be reduced by 5 days during NF and DF future climatic scenarios. Similar trend is reflected across generation wise also. The reduction of generation time was evident at first generation of *S. litura* during NF (29 days) and DF (26 days) scenarios than BL period (33 days) and reduction of generation time was would occur in second and third generations also.

The average life cycle of *S. litura* was found to be 30 and 29 days during BL period and PR climatic conditions

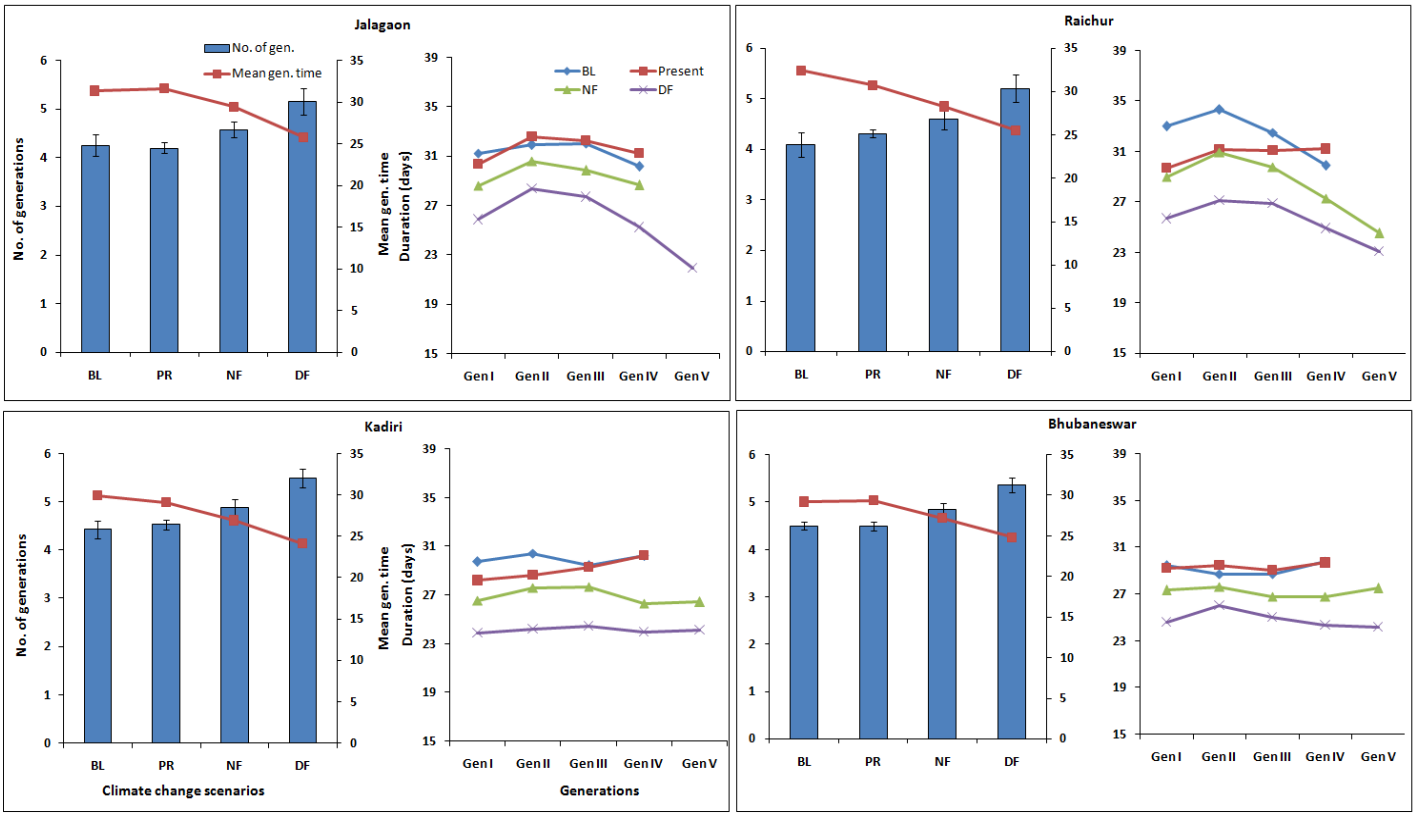

Figure 1. Variation in number of generations and mean generation time of *S. litura* on peanut under CCS.

at Kadiri and Bhubaneswar locations. The shortened life cycle of 27 and 25 days indicating the reduction of life cycle by 3 and 4 days was expected in NF and DF climatic scenarios, respectively. Similarly, inter-generic variation is concerned with the shortened life cycle in first generation of insect that represented a duration of 24 days in DF and 27 in NF than 30 days in BL period at Kadiri location and parallel reduction of generation timeat Kadiri and Bhubaneswar locations. The shortened life cycle of 27 and 25 days indicating the reduction of life cycle by 3 and 4 days was expected in NF and DF climatic scenarios, respectively. Similarly, inter-generic variation is concerned with the shortened life cycle in first generation of insect that represented a duration of 24 days in DF and 27 in NF than 30 days in BL period at Kadiri location and parallel reduction of generation time was expected to take place with second and third generations also. At Bhubaneswar, the generation time across all generations varied from 24 to 28 days and accelerated development is expected with shortened life cycle during both future climate change scenarios. Inter-generic variation across 4 to 5 generations was evident and the number of days per generation in NF and DF climate change scenarios is expected to be shortened by 2 and 5 days, thereby a significant advancement of completion of life cycle was predicted, resulting in more number of generations (5) at all seven locations.

The percent reduction of generation time of *S. litura* at corresponding locations during NF and DF scenarios over BL along with present period was depicted in Figure 2. It was predicted that the percent decrease would be higher during (14 to 22%) DF and (3 to 11%) NF scenarios over BL period indicating the shortened life cycle than BL period to accommodate the more number of generations under CCS.

It is well known that accelerated development of insect**s** is possible due to increased temperature which would result in more cycles of generations / crop losses during the season or year. Prediction of developmental time or mean generation time of insect pests in relation to temperature can be an important tool for pest management (Roy et al., 2002). Insects develop more rapidly during periods of time with suitable warmer temperatures. Increased temperature will accelerate the development of insects possibly resulting in more cycles of generations per year. It s predicted that the projected climate warming would influence the multivoltine species in different ways at different magnitudes. Insects of Aphididae and some Lepidoptera, e.g. *Pieris brassicae*, which are multivoline in nature, undergo faster

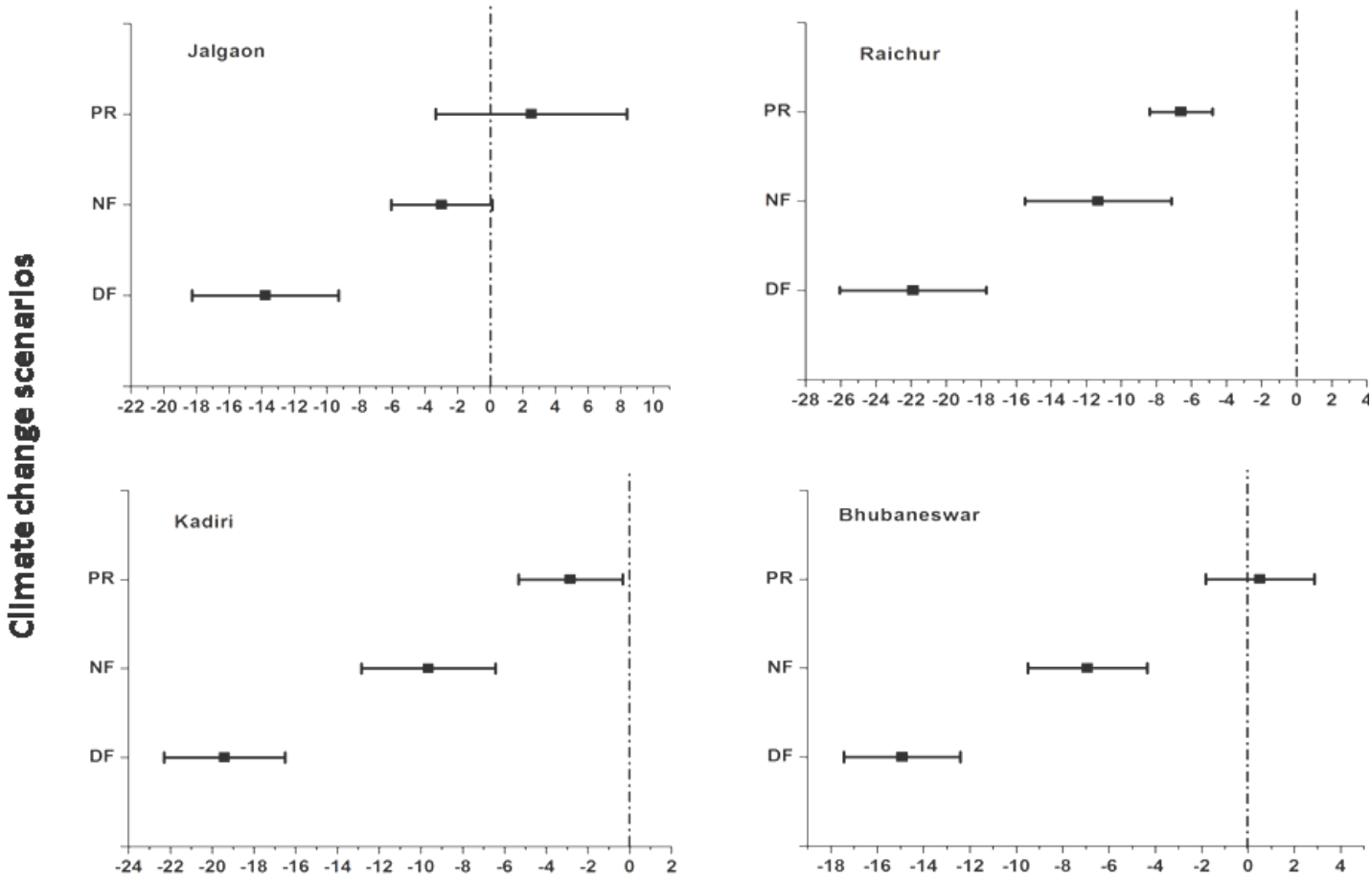

Figure 2. Per cent change in generation time (days) of *S. litura* on peanut under CCS over Baseline period.

development time at higher temperatures, allowing for additional generations within a year (Pollard and Yates, 1993). Many of these species will expand their geographical ranges to higher latitudes and altitudes, as has already been observed in a number of common butterfly species (Parmesan et al., 1999). The occurrence of insect population varies from year to year and its dynamics can be predicted using the approach of Growing Degree-days (GDD).

Predictions of *S. litura* development on peanut were attempted under current (BL and PR periods) and expected future climate change (near and distant future) scenarios. The cumulated thermal heat units were expressed as degree days (DD); the number of generations and mean generation time of *S. litura* were estimated through selection of seven representative peanut growing locations of India. Locations like Raichur, Jalgaon, Bhubaneswar and Kadiri were compared for inter-state and Hayathnagar, Tirupati and Jagityal were selected for intra-state (AP) differences. The influence of temperature on development and survival of *S. litura* would affect the population dynamics of pest and such influence can be estimated and quantified by calculating the number of generations. The findings of the present study shows that one additional generation would occur at majority of locations during future climatic scenarios. The insect was predicted to have significant advancement of completion of life cycle, resulting in more number of generations (5) at all seven locations.

Production of more number of generations annually with extreme temperatures in case of majority of insect species was well known and this phenomenon becomes regular with gradual warming (Lastuka, 2008) and our results add *S. litura* on peanut in India to the list as a case in point. The information on occurrence of additional generations with increase in temperature was well documented across various insect orders *viz*; lepidopterans - *Nephotettix cincticeps* (Yamamura et al., 2006), *Plutella xylostella*, (Kiritani, 2006), *Cydia pomonella* (Marchioro and Foerster, 2011; Hirschi et al., 2012), *Phthorimaea operculella* (Abolmaaty et al., 2011) and other orders (Khalil et al., 2010; Hlasny et al., 2011). It was found that a substantial proportion of the 263 multivoltine lepidopteran species in his dataset exhibited

an increased frequency of second and subsequent generations since 1980, with 44 species displaying a stable increase in the number of generations after 1980 (Altermatt, 2010). Our findings are in corroboration with those of earlier reviews, indicating that the insects respond to higher temperature with increased rates of development, more number of generations with less time between generations (Das et al., 2011).

Current investigations for locations from seven different agro-ecological zones of the country (inter and intra state level differences) have shown significant variation in developmental time, number of generations and thermal requirements of *S. litura* on peanut. While these results consider the effect of temperature only, other factors such as host plant response to changing climate, thermal adaptation and rainfall distribution may also influence the rate of insect development. Rise in temperature boosts the carrying capacity of the insect species and thus gives scope for more numbers of generations and individuals (Messer, 2013).

The additional number of generations of *S. litura* on peanut across locations of Indian condition implies the direct and definitive impact of projected increasing in temperature in the near and distant future climate change scenarios. On the other hand, the effects of such increased temperature combined with CO_2 on increasing the biomass of peanut crop may offset the damage caused by *S. litura*. Nevertheless, peanut pest management can always account for the anticipated higher number of generations in the future. Further studies of crop phenology, pest (*S. litura*) phenology and multi-species interactions including *S. litura* parasitoid associations under CCS would aid in understanding the confounding climatic impacts comprehensively besides being prepared for a better decision making on peanut plant protection.

Conflict of Interests

The author(s) have not declared any conflict of interests.

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Scientific Research and Essays

Full Length Research Paper

Antidiabetic activity and phytochemical screening of *Acalypha wilkesiana* (Euphorbiaceae) Mull Arg. roots in alloxan-induced diabetic rats

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The aim of this study was to investigate the anti-diabetic effects and biochemical parameters of methanol root extract of *Acalypha wilkesiana* Mull Arg. (MEAW) in alloxan-induced diabetic rats. The effect of the extract (200 and 400 mg/kg, *p.o.*) on fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) level and liver glycogen content were investigated in alloxan-induced diabetic rats after 14 days. An oral glucose tolerance test (OGTT) was also performed on the diabetic rats. Dose selection was made on the basis of acute oral toxicity study. Phytochemical analysis of the root extract was carried out following standard procedures. The most significant ($p<0.05$) reduction of FBG level of 74.06% was observed for 400 mg/kg in alloxan induced diabetic rats. A significant reduction ($p<0.05$) in serum TC and TG level of 50.43 and 58.05% respectively was also observed for the high dose of the extract. The SGOT and SGPT levels were significantly ($p<0.05$) reduced. The MEAW also showed improvement of body weight in diabetic rats. The animals showed no mortality at a dose of 5000 mg/kg while results of phytochemical analysis revealed the presence of mainly alkaloids, terpenoids, flavonoids, saponins, steroids and tannins. These results show that the root of *Acalypha wilkesiana* possesses antidiabetic, antihyperlipidemic and hepatoprotective effects.

Key words: *Acalypha wilkesiana,* cholesterol, fasting blood glucose, oral glucose tolerance test (OGTT), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), triglyceride.

INTRODUCTION

Today, medicinal plants are increasingly being used in most parts of the world as: Hypolipidemic (Yadav et al, 2008), contraceptive, abortifacients, emmenagogues or oxytocic (Ritchie, 2001), antihypertensive (Nworgu et al., 2008), treatment of skin diseases (Ajose, 2007), antimicrobial (Okwu and Uchegbu, 2009) and hypoglycemic (Osadebe et al., 2004; Ezugwu et al., 2005; Patel et al., 2008; Yadav et al., 2008; Odoh et al., 2013). Hypoglycemic agents from plants have been used in the management of diabetes mellitus.

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Diabetes mellitus (DM) is a multifactorial disorder which is characterized by hyperglycemia, lipoprotein abnormalities, raised metabolic rate, defect in reactive oxygen species scavenging enzymes and altered intermediary metabolism of major food substances (Scoppola et al., 2001). Diabetes is a major degenerative disease in the world today, affecting at least 15 million people and having complications which include hypertension, atherosclerosis and microcirculatory disorders (Edem, 2009). There has been increasing demand for the use of plant products with antidiabetic activity. The high cost, low availability, uncertainty of use during pregnancy and undesirable side effects of synthetic drugs have been some of the factors leading to a strong preference for hypoglycemic drugs of plant origin, which are believed to be suitable for chronic treatments (Okigbo and Mmeka, 2006).

Acalypha wilkesiana belongs to the family Euphorbiaceae. The common names are copperleaf, Joseph's coat, fire dragon, beef steak plant and match-me-if-you-can (Christman, 2004). The Hausas of Northern Nigeria call it "Jiwene" and "Jinwinini", while the Yorubas of Southern Nigeria call it "aworoso" (Ikewuchi et al., 2010). Aqueous leaf extract of *A. wilkesiana* is traditionally used to treat neonatal jaundice in western part of Nigeria on short-term basis. The plant is popularly used for the treatment of malaria, dermatological disorders, gastrointestinal disorders (Akinde and Odeyemi, 1987). It is widely used in southern Nigeria as a remedy for the treatment of undefined skin infections in children (Alade and Irobi, 1992). The antihypertensive (Nworgu et al., 2011) and antimicrobial (Gotep et al., 2010) properties of the plant have been reported. The antihyperglycemic, antihyperlipidemic and ameliorative role on electrolytes disturbances of the leaf extract have been demonstrated in streptozotocin-induced diabetic mice (Al-Attar, 2010). The present study aims to screen plant phytochemically, further investigate the antidiabetic and biochemical parameters of the root extract of the plant in alloxan-induced diabetic rats and in oral glucose tolerance test models.

MATERIALS AND METHODS

Collection and preparation of plant material

The roots of *A. wilkesiana* were collected from Orba area in Nsukka District, Enugu State, Nigeria in November, 2012 and authenticated by Mr. A. O. Ozioko, a taxonomist with International Centre for Ethnomedicine and Drug Development (InterCEDD). A voucher herbarium specimen No.PCG/12/415 was preserved in the Department of Pharmacognosy and Environmental Medicines, University of Nigeria Nsukka, Nigeria. The collected roots were dried under shade and powdered to a coarse consistency in a grinder mill. The powder was passed through 40 # mesh particle size 0.422 mm. Exactly 500 g of this powder was packed into a soxhlet apparatus and extracted exhaustively with methanol to obtain the methanol extract. This was concentrated *en vacuo* and the methanol extract (MEAW, yield: 21.80% w/w) was preserved in a refrigerator and used for subsequent assays.

Animals

Adult albino Wistar rats (175 to 210 g) of both sexes were procured from the Faculty of Veterinary Medicine, University of Nigeria, Nsukka, Nigeria and housed in the University's Animal House in the Department of Pharmacology and Toxicology. They were fed with standard rat pellet diet (Topfeeds PLC, Nigeria). The experimental protocols were in accordance with the guidelines of the Ethics Committee of the University of Nigeria (approved ref: NHREC/05/01/2008B). The care and handling of animals was in line with the internationally accepted principles for laboratory animal use and care as found in the European Community guidelines (86/609/EEC) (EEC, 1986).

Chemicals

The chemicals used in the study were: alloxan monohydrate (Spectrochem Pvt. Ltd, Mumbai), glibenclamide (Aventis Pharma Ltd, Verna, Goa), dextrose (Emkay Labs, Mumbai), Tween 80 (S.D. Fine-Chem Ltd, Mumbai), and anesthetic ether (Ozone International, Mumbai). All other chemicals and reagents used were of analytical grade.

Acute toxicity study (LD_{50})

The oral acute toxicity of the MEAW was determined in mice as described by Lorke (1983). Nine mice randomly divided into three groups (n=3) were orally administered 10, 100 and 1000 mg/kg of MEAW respectively, and observed for 24 h for mortality. When no death occurred, 1600, 2900 and 5000 mg/kg of MEAW was administered to a fresh batch of animals (n=1) and the number of death in 24 h also noted. The LD_{50} was estimated as the geometric mean of the highest non-lethal dose and the lowest lethal dose.

Induction of diabetes

Diabetes was induced by intraperitoneal injection of 120 mg/kg of a solution alloxan monohydrate (Kannur et al., 2006). The alloxanized rats were kept for 7 days with free access to food and water. On the 8^{th} day, the rats were fasted for 12 h but allowed free access to water and their fasting blood sugar (FBS) level was determined using Accu-chek® active glucometer (Roche Diagnostic Corporation, Mannheim, Germany) and blood glucostrips (Roche Diagnostic Pvt Ltd, Mumbai)). The animals were carefully monitored every day. Rats with glucose levels above 200 mg/dl were used for the study.

Antidiabetic study in normal and diabetic rats (FBS)

The non-diabetic rats were randomly divided into four groups (n = 6). Group 1 received 2 ml/kg of 5% Tween 80 while group 2 received 5 mg/kg glibenclamide. Groups 3 and 4 received 200, 400 mg/kg of the MEAW respectively. Same procedures were performed using diabetic rats at similar doses of MEAW. All groups received various treatments orally. Blood samples were drawn at weekly intervals from the tail vein after overnight fast till the end of study. FBS levels were estimated on day 0, 7 and 14 of the study (Claudia et al., 2006). On day 14, under mild ether anesthesia blood was collected and processed for estimation of serum glucose and serum lipid profile as described below.

Collection of blood and estimation of biochemical parameters

On day 14, blood was collected from retro-orbital venous plexus of the rats under light ether anesthesia using capillary tubes into Eppendorf tubes containing heparin. The plasma was separated by centrifugation for 5 min at 5000 rpm and was analyzed for lipid profiles (serum cholesterol, serum triglyceride), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) and liver glycogen content. The plasma profiles were measured by standard enzymatic methods with an automatic analyzer (Phuong et al., 2004).

Estimation of glycogen content in liver

Glycogen content in liver was measured according to spectrophotometric determination of glycogen with o-toluidine reagent. It utilizes the o-toluidine glucose coupling reactions for the estimation of glycogen after trichloroacetic acid extraction, precipitation by alcohol and hydrolysis (Khan et al., 2010).

Body weight measurement

Body weight was measured totally four times during the course of study period (Nagappa et al., 2003), before alloxan induction (initial values), and on day 1, 7 and 14 of the treatment period, using a digital weighing scale (KERN (EMB), Tischwaage, Germany).

Oral glucose tolerance test (OGTT) in normal rats

Animals were divided into four groups of six rats each. Group 1 was kept as vehicle control which received 5% Tween 80 (p.o.). Group 2 received glibenclamide (5 mg/kg) as the reference standard while Group 3 and 4 received MEAW 200 and 400 mg/kg respectively. Blood sugar level was determined from overnight fasted animals at 0 min. After 30 min of the drug treatment, animals were fed with glucose (4 g/kg) and blood glucose was determined at 1/2, 1, 2, and 3 h after glucose load (Sellamuthu et al., 2009).

Qualitative/quantitative phytochemical analysis

Alkaliods determination

The determination was as described by Harborne (1973). 5 g of sample was weighed into a 250 ml beaker and 200 ml of 10% acetic acid in ethanol was added, covered and allowed to stand for 2 h. This was filtered and the extract was concentrated on a water bath to one–quarter of the original volume. Concentrated NH_4OH was added drop wise to the extract and the precipitate was collected and washed with dilute NH_4OH and then filtered. The alkaloid (residue) was dried and weighed.

Flavonoids determination

Following the method described by Boham and Kocipai- Abyazan (1994), 10 g of the sample was extracted repeatedly with 100 ml of 80% aqueous methanol at room temperature. The whole solution was filtered through a Whatman filter paper No 42 (125 mm). The filtrate was later transferred into a crucible and evaporated to dryness over a water bath and weighed to a constant weight.

Tannins determination

Tannin determination was done by Van-Burden and Robinson (1981) method. 500 mg of the sample was weighed into a 50 ml plastic bottle. 50 ml of distilled water was added and shaken for 1 h on a mechanical shaker. This was filtered into a 50 ml volumetric flask and made up to mark. 5 ml of the filtrate was pipette out into a test tube and mixed with 2 ml of 0.1 M $FeCl_3$ in 0.1 N HCl and 0.008 M potassium ferrocyanide. The absorbance was measured at 120 nm within 10 min.

Cardiac glycosides determination

Cardiac glycoside content in the sample was evaluated using reagent as described by El-Olemy et al., (1994). 1 g of the fine powder was soaked in 10 ml of 70% alcohol for 2 h and then filtered. The extract obtained was then purified using lead acetate and Na_2HPO_4 solution before the addition of freshly prepared Buljet's reagent (containing 95 ml aqueous picric acid + 5 ml 10% aqueous NaOH). The difference between the intensity of colours of the experimental and blank (distilled water and Buljet's reagent) samples gives the absorbance and is proportional to the concentration of the glycosides.

Saponins determination

The method employed was that of Obadoni and Ochuko (2001). 20 g of the sample was put into a conical flask and 100 ml of 20% aqueous ethanol was added. The sample was heated over a hot water bath for 4 h with continuous stirring at 55°C. The mixture was filtered and the residue re-extracted with 200 ml of 20% ethanol. The combined extracts were reduced to 40 ml over water bath at 90°C. The concentrate was transferred into a 250 ml separating funnel and 20 ml of diethyl ether was added and shaken vigorously. The aqueous layer was recovered while the ether was discarded. The purification process was repeated. 60 ml of n-butanol was added. The combined n-butanol extracts were washed twice with 10 ml of 5% aqueous NaOH. The remaining solution was heated on a water bath. After evaporation the samples were dried in the oven to a constant weight. The saponin content was calculated as percentage weight.

Terpenoids determination

50 g of the powdered sample was extracted with solvent combination of methanol and water (4:1) at room temperature for 24 h. The solution was filtered using Whatman filter paper No. 1 and the filtrate was then evaporated to 1/10 volume at 40°C. The evaporated filtrate was acidified with 2 M sulphuric acid (pH 0.89) followed by chloroform extraction (three times the volume), stirred and allowed to stand in a separating funnel. Out of the two layers formed, the non-aqueous layer was taken and evaporated till dryness. The dried extract contained components like terpenoids which were further used for thin layer chromatography analysis (Harbourne, 1984).

Steroids determination

1 ml of a methanolic solution of the MEAW was transferred into 10 mL volumetric flasks. Sulphuric acid (4 N, 2 ml) and iron (III) chloride (0.5% w/v, 2 ml), were added, followed by potassium hexacyanoferrate (III) solution (0.5% w/v, 0.5 ml). The mixture was heated in a water-bath maintained at 70 ± 2°C for 30 min with occasional shaking and diluted to the mark with distilled water. The absorbance was measured at 780 nm against the reagent blank (Tyler, 1994).

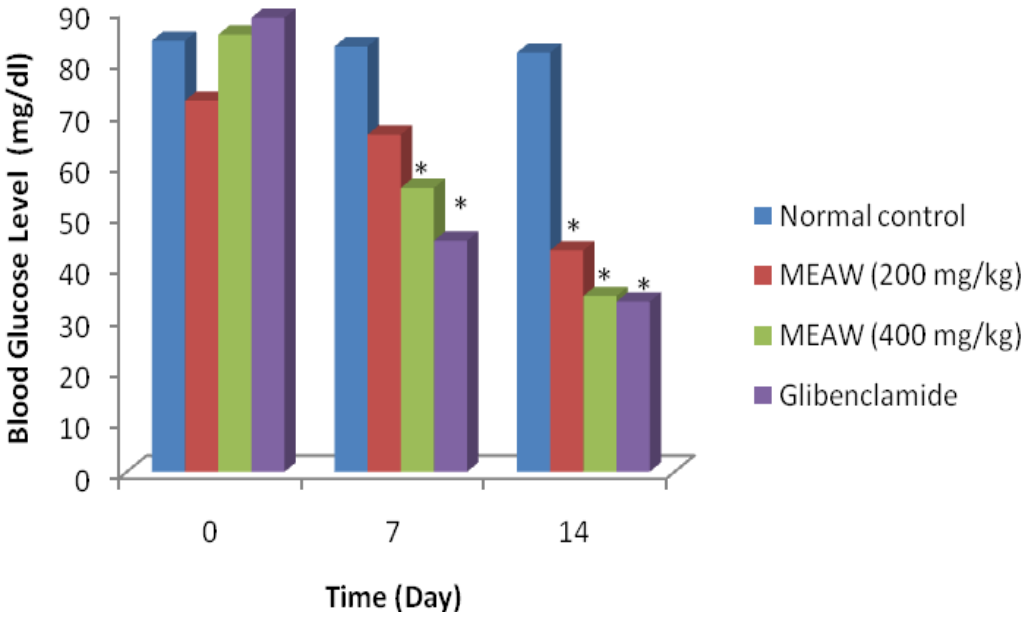

Figure 1. Effect of MEAW root and glibenclamide on FBS levels (mg/dl) of normal rats for 2 weeks.

Statistical analysis

The values are expressed as mean ± SEM (standard error of the mean). The results were analyzed for statistical significance using one-way ANOVA followed by Dunnet's test. $P < 0.05$ was considered significant.

RESULTS AND DISCUSSION

In acute toxicity study, the extract was found to be safe at the tested dose level of 5000 mg/kg b. wt. The safety of the extract is the basis for the choice of the doses of the extract in this study. Previous study has shown that oral administration of the plant leaf extract at high dose of 10,000 mg/kg daily for 14 days does not produce any mortality in rats. All animals display normal behavioral, neurological and autonomic profiles (Iniaghe et al., 2013).

To ascertain a scientific base for the usefulness of this plant in the treatment of diabetes, it was decided to evaluate experimental design of antidiabetic activity by following normal, alloxan-induced and glucose tolerance test models. In the normoglycemic animals, the extract administration for 14 days produced a marked reduction in the FBS of the animals in a dose-related fashion and the effect was comparable to that of glibenclamide (Figure 1). The extract and glibenclamide caused hypoglycemia (<40 mg/dl) in the animals after 2 weeks of administration. It has been reported that provided the β-cells are fully functional, sulphonylureas, such as glibenclamide, can cause hypoglycemia since insulin release is initiated even when glucose concentrations are below the normal threshold for glucose-stimulated insulin release (approximately 5 mmol/L or 90 mg/dL) (Krentz and Bailey, 2005). This suggests that the plant may have similar mode of action to glibenclamide, an insulin secretagogue, with respect to blood glucose lowering effect.

Compared with the diabetic animals, the extract-treated groups exhibited remarkable lowering in the elevated blood glucose levels (Figure 2) in a dose-related fashion. The 400 mg/kg dose produced higher reduction (74.06%) than the 200 mg/kg dose (67.81%). The effect of the 400 mg/kg of the extract was similar to that of glibenclamide which brought back the blood glucose to normal values after 14 days. It has been suggested that the *A. wilkesiana* leaf extract might possess insulin like effect on peripheral tissues either by promoting glucose uptake and metabolism or inhibiting hepatic gluconeogenesis (Al-Attar, 2010).

Effective blood glucose control is the key for preventing or reversing diabetic complications and improving quality of life in patients with diabetes. Thus sustained reduction in hyperglycemia will decrease the risk of developing microvascular complications and most likely reduce the risk of macrovascular complications (Muniappan et al., 2004). On the basis of this statement we have selected the glucose-induced hyperglycemic model to screen the anti-hyperglycemic activity of the plant extract. Any drug that is effective in diabetes will have the ability to control the rise in glucose level by different mechanisms and the ability of the extract to prevent hyperglycemia could be determined by glucose- loaded hyperglycemic model (Senthilkumar et al., 2011). In the glucose-loaded hyperglycemic (OGTT) model, the plant exhibited significant ($p<0.05$) antihyperglycemic activity which was more at a dose level of 400 mg/kg (Figure 3).

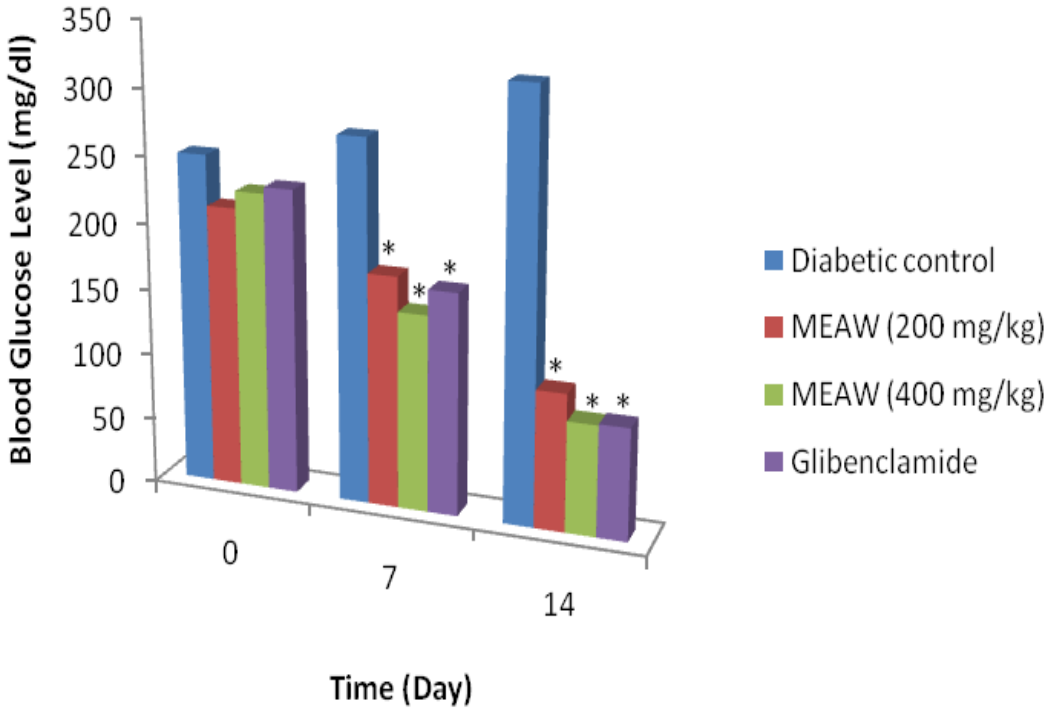

Figure 2. Effect of MEAW root and glibenclamide on FBS levels (mg/dl) of diabetic rats for 2 weeks.

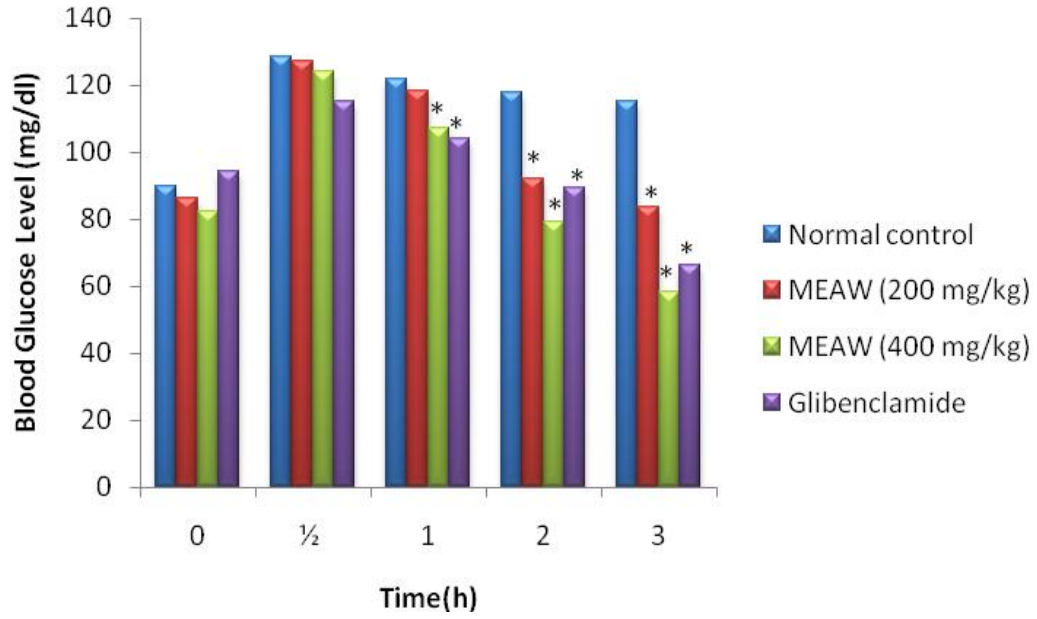

Figure 3. Effect of MEAW root on glucose loaded hyperglycemic rats (OGTT).

Remarkable blood glucose lowering effect was observed from 2 to 3 h post extract administration. At ½ h after glucose administration, the peak of blood glucose level increased rapidly from the fasting value and then subsequently decreased. Excessive amount of glucose in the blood induces insulin secretion. This secreted insulin will stimulate peripheral glucose consumption and control the production of glucose through different mechanisms (Andrew, 2000). Oral glucose tolerance test (OGTT) measures the body's ability to use glucose, the body's

Table 1. Effect of MEAW on the biochemical parameters of alloxan-induced diabetic rats after 14 days of treatment.

Group	Parameter			
	Total cholesterol (mmol/L)	Triglycerides (mmol/L)	SGOT (AST) (iu/L)	SGPT (ALT) (iu/L)
Normal control	33.00 ± 2.05	36.20 ± 0.22	30.00 ± 0.30	19.00 ± 2.18
Diabetic control	82. 40± 3.01	113.60 ± 0.14	47.30± 3.60	35.70 ± 1.09
Glibenclamide	35.36 ± 1.20*	40.60 ± 1.06*	35.60± 1.15*	28.18±1.33*
MEAW(200 mg/kg)	49.90 ± 0.42*	79.20 ± 0.92*	40.60± 1.15*	30.05±1.33*
MEAW(400 mg/kg)	36.50 ± 2.14*	45.70 ± 3.10*	32.20±2.16*	21.20±0.01*

Each value represents the mean ± SEM of five observations. *P < 0.05, Vs diabetic control (ANOVA followed by Dunnett's test); MEAW, Methanol extract of *Acalypha wilkesiana* , SGOT – serum glutamate oxaloacetate transaminase; SGPT, serum glutamate pyruvate transaminae.

main source of energy. It can be used to diagnose pre-diabetes and diabetes. In this study, it is found that the MEAW has hypoglycemic effect in glucose induced hyperglycemic rats, thus further giving credence to the antidiabetic effect of the plant.

The effects of the plant extract on the lipid profile and serum enzymes are presented in Table 1. The diabetic rats showed hypercholesterolemia and hypertriglyceridemia but the treatment with MEAW significantly ($p<0.05$) decreased both cholesterol and triglyceride levels with percentage reduction of 50.43 and 58.05% respectively (by the 400 mg/kg dose of the extract). The levels of serum lipids are usually elevated in diabetes mellitus and such an elevation represents a risk factor for coronary heart disease. Similar elevations in the serum triglycerides and cholesterol have been obtained in different experimental models (Al-Attar, 2010; Salahuddin et al., 2010). This abnormal high level of serum lipids is mainly due to the uninhibited actions of lipolytic hormones on the fat depots mainly due to the action of insulin (Pushparaj et al., 2007). Under normal circumstances, insulin activates the enzyme lipoprotein lipase, which hydrolyses triglycerides. However, in diabetic state lipoprotein lipase is not activated due to insulin deficiency resulting in hypertriglyceridemia (Pushparaj et al., 2007). Also insulin deficiency is associated with hypercholesterolemia. Insulin deficiency may be responsible for dyslipidemia, because insulin has an inhibitory action on HMG-CoA reductase, a key rate-limiting enzyme responsible for the metabolism of cholesterol-rich LDL particles. The mechanisms responsible for the development of hypertriglyceridemia and hypercholesterolemia in uncontrolled diabetes in humans are due to a number of metabolic abnormalities that occur sequentially (Murali et al., 2002). This implies that MEAW can prevent or be helpful in ameliorating the complications of lipid profile seen in some diabetics in whom hyperglycemia and hypercholesterolemia coexist quite often (Sharma et al., 2003).

In the diabetic rats there was a significant rise in SGOT and SGPT levels in comparison to normal rats, which could relate to excessive accumulation of amino acids (glutamate and alanine) in the serum of diabetic animals as a result of amino acids mobilization from protein stores (Colev et al., 1994) (Table 1). The higher levels of SGOT and SGPT, may give rise to a high concentration of glucose. In other words, the gluconeogenic action of SGOT and SGPT plays the role of providing new supplies of glucose from other sources such as amino acids. Following administration of the plant extract, SGOT and SGPT levels were significantly ($p<0.05$) reduced in a dose-related fashion with 400 mg/kg dose of the extract exhibiting a more significant effect.

In the present study, it was found that the level of glycogen in liver was reduced in diabetic rats when compared to the normal control group (Figure 4). Induction of diabetes with alloxan was associated with decrease in hepatic glycogen, which could be attributed to the decrease in the availability of the active form of the enzyme, glycogen synthetase, possibly because of low levels of insulin (Goel et al., 2004). Treatment of diabetic rats with glibenclamide and the extract improved the level of glycogen content remarkably in relation to the diabetic control group. *A. wilkesiana* restored the depressed hepatic glycogen levels possibly by increasing the level of insulin. Decreased activities of the enzymes involved in glucose homeostasis in liver and kidney such as hexokinase has been reported in diabetic animals resulting in depletion of liver and muscle glycogen content (Grover et al., 2000). It is possible that treatment with the plant extracts might increase the level of enzyme to the control level indicating an over-all increase in glucose influx.

The effect of the plant extract on the body weight of the diabetic animals is shown in Figure 5. Treatment with the plant extract improved the average body weights of rats indicating control over polyphagia and muscle wasting due to hyperglycemic condition. The diabetic rats had lower body weights as compared to the normal rats. In spite of the increased food consumption, loss of body weight due to defect in glucose metabolism and excessive breakdown of tissue protein is a characteristic condition in diabetics.

Phytochemical screening of the MEAW showed the

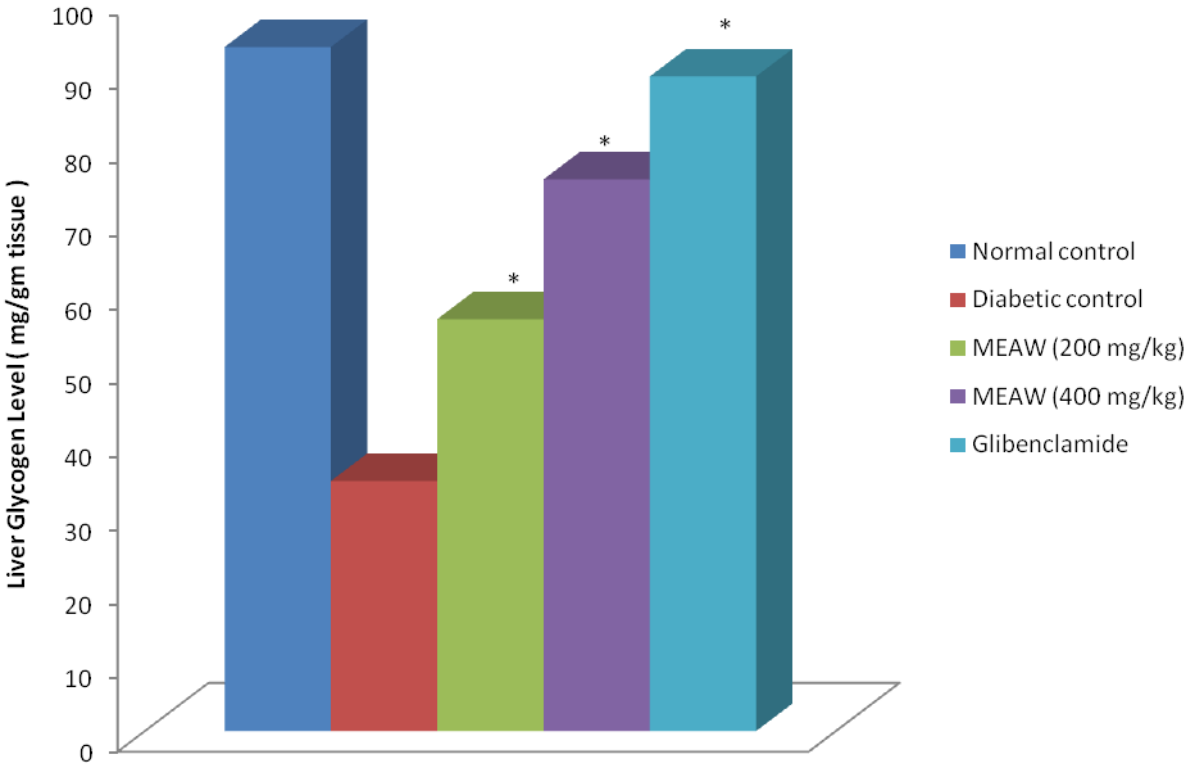

Figure 4. Effect of MEAW on the glycogen level in liver of diabetic rats.

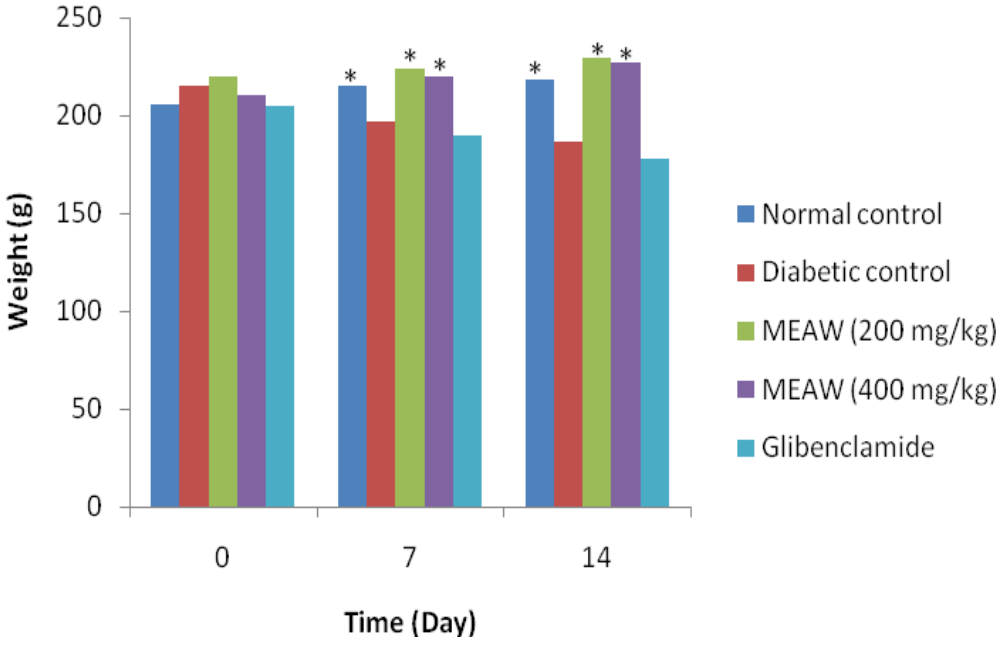

Figure 5. Effect of MEAW on the body weight of rats.

presence of various chemical constituents, including alkaloids, saponins, triterpenoids, flavonoids, tannins and steroids (Table 2) which may be responsible for its antidiabetic properties. Alkaloids (128.90±0.40 mg/100g) and terpenoids (115.5±1.20 mg/100 g) are more abundant while cardiac glycosides are lowest (0.652±1.48

Table 2. Results of quantitative phytochemical analysis of *A. wilkesiana* roots.

Constituents	Value (mg/100 g)[a]
Alkaloids	128.90 ± 0.40
Flavonoids	6.417 ± 0.22
Tannins	6.055 ± 1.08
Cardiac glycosides	0.652 ± 1.48
Saponins	9.780 ± 0.55
Steroids	16.4 ± 0.30
Terpenoids	115.5 ± 1.20

[a]Values are mean ± SEM of three replicate analyses.

mg/100 g). Similar phytoconstituents have been obtained from the leaves of this plant (Ikewuchi et al., 2010). Flavonoids are known for their diverse biological activities including hypoglycemic and hypolipidemic activities resulting from their antioxidant activity (Afanas'ev et al., 1995). Tannins have been reported to reduce blood cholesterol (Basu et al., 2007). It could be conceived that any of these biomolecules may sensitize the insulin receptor or stimulate the β-cells of islets of langerhans to release insulin which may finally lead to improvement of carbohydrate metabolizing enzymes towards the re-establishment of normal blood glucose level. The significant antidiabetic effect of methanol extract of *A. wilkesiana* in alloxan diabetic rats may also be due to enhanced glucose utilization by peripheral tissues. It is also possible that any of these phytochemicals could be associated with the antihyperlidipemic effect of the plant. The antihyperlipidaemic effect might have resulted from decreased fatty acid concentration in the circulation and reduced cholesterol synthesis possibly due to the flavonoid constituents of the plant extract (Ojewunmi et al., 2014). The actual mechanism of action and the phytoconstituent responsible for the observed effects of the plant, however, needs to be investigated further.

Conclusion

We conclude that the methanol extract of *A. wilkesiana* roots has potent antidiabetic effects in alloxan-induced diabetic rats. The extract also possesses ameliorating effect on the lipid profile and other biochemical parameters in diabetic rats. The present investigation has also opened avenues for further research especially with reference to the development of potent formulation for diabetes mellitus from the roots of *A. wilkesiana*. Activity guided fractionation and its evaluation is in progress in our laboratory.

Conflict of Interest

The author(s) have not declared any conflict of interests.

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