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About the journal

The journal aims to address issues related to the third sector and community-based activities. The magazine therefore has the aim of spreading the culture of the third sector (voluntary organizations, social promotion associations, philanthropic bodies, social enterprises, mute aid companies, recognized and non-recognized associations, ecclesiastical bodies), the topics of interest are:

Social services

Health interventions and services

Education, health education and training

Safeguarding and improving environmental conditions

Protection and enhancement of cultural and landscape heritage

University and post-university education

Organization and management of cultural, artistic or recreational activities of social interest

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Tourist activities of social, cultural or religious interest

Extra-curricular training, aimed at preventing early school leaving and at school and training success, at preventing bullying and combating educational poverty

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Services aimed at introducing or reintegrating workers and disadvantaged people into the labour market

Social housing

Humanitarian Reception

Social agriculture

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Promotion of the culture of legality, peace between peoples, nonviolence and unarmed defence

Promotion and protection of human, civil, social and political rights, as well as the rights of consumers and users of activities of general interest

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**COVID-19, paradossi e nuovi modelli di business.
Un'opportunità per il terzo settore?**

**COVID-19, paradoxes, and new business models. An opportunity
for third sector organizations?**

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Abstract

The Covid-19 pandemic has impacted several business fields, besides the healthcare sector. The new situation calls for new challenges, with several organizations needing to rethink their business models. Using an EFTE (estimate, feedback, talk, estimate) approach, the article presents 50 paradoxes to rethink post-pandemic business models, highlighting those most suitable for third sector organizations.

Keywords: Business models, third sector organizations, Covid-19

Abstract

La pandemia Covid-19 ha avuto degli impatti in molti settori, oltre che in quello sanitario. Numerose sono le realtà chiamate ad affrontare nuove sfide, dovendo ripensare ai propri modelli di business. Utilizzando un approccio EFTE (estimate, feedback, talk, estimate), il documento presenta 50 paradossi per ripensare i modelli di business post- pandemia, mettendo in luce quelli che più si adattano al terzo settore.

Parole chiave: Modelli di business, terzo settore, Covid-19

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1. Introduzione

La pandemia Covid-19, emergenza sanitaria pubblica di rilevanza internazionale (WHO, 2020), ha avuto degli impatti in molti settori, oltre che in quello medico-sanitario (Campra, M., Esposito, P., Brescia, 2021; Cobianchi *et al.*, 2020; Donthu and Gustafsson, 2020). Tra le numerose conseguenze, l'Italia, come molti altri Paesi, ha risentito della chiusura forzata di numerose attività commerciali e manifatturiere non essenziali (Buccino, 2020; Centra, M., Filippi, M., Quaranta, 2020), a cui si è aggiunto il divieto di spostarsi e viaggiare (Angeloni, 2021; Biancone *et al.*, 2020). Il nostro Paese è stato uno dei primi a dover affrontare il virus e lo tsunami economico-sociale da esso creato (Grasselli *et al.*, 2020; Pisano *et al.*, 2020; Romani *et al.*, 2020, 2021), andando a sommarsi negativamente ad una situazione già non particolarmente florida dovuta agli strascichi della crisi internazionale del 2008/2009.

In questo contesto, anche il terzo settore ha risentito negativamente delle restrizioni normative conseguenti la pandemia. Se alcune organizzazioni, pensiamo a quelle che gravitano intorno al settore sanitario, hanno potuto continuare le proprie attività, fungendo anzi da supporto essenziale all'ente pubblico impegnato ad affrontare l'emergenza sanitaria, altre hanno dovuto interrompere le proprie azioni in ottemperanza delle restrizioni in materia di distanziamento sociale. La pandemia da COVID-19 ha quindi avuto un effetto pesante anche sulle organizzazioni del terzo settore, e di conseguenza su tutti coloro che traggono un prezioso supporto da tali enti.

Tuttavia, paradossalmente, le pandemie e le calamità naturali, in genere, si sono dimostrate anche capaci di cambiare il corso della storia, diventando la spinta per il cambiamento di sistemi politici, economici e tecnologici.

Si tratta di un vero e proprio paradosso, che mette assieme, effetti dannosi e propizi, senza che uno porti all'esclusione dell'altro (Bagnoli *et al.*, 2020).

Questa crisi può essere quindi sfruttata per puntare a dei cambiamenti, attraverso il metodo dei paradossi. Le aziende e le organizzazioni pubbliche e private devono, a questo fine, individuare i paradossi strategici presenti, cercando di cogliere la spinta per innovare il proprio modello di business, ossia il modo in cui un'azienda crea, cattura e distribuisce valore per i propri clienti e, in generale, i propri portatori di interesse (Osterwalder *et al.*, 2005; Osterwalder and Pigneur, 2010). Le strategie aziendali che portano a scegliere uno dei poli apparentemente opposti che caratterizzano un paradosso nascondono la reale complessità del contesto competitivo, risultando, quindi, poco utili per vincere la competizione. Questa situazione è gestibile solo adottando un approccio che porti ad unire, attraverso un processo circolare, i due poli, che finiscono per fungere uno da attrattore per l'altro, generando così una dinamica equilibrata e supportando la creazione creativa di nuovi modelli di business (Bagnoli *et al.*, 2021).

Questo elaborato punta a gestire le scelte paradossali per approfondire il processo di gestione strategica di una crisi, dando particolare attenzione a quei paradossi che più si adattano al terzo settore (Brescia, 2020), come associazioni, gruppi di volontariato, cooperative e imprese sociali, che anche se non messi in luce come le imprese, sono stati colpiti da provvedimenti conseguenti la pandemia, dovendo ora gestire situazioni dinamiche e differenti rispetto al recente passato. Il presente lavoro fa parte di una più ampia riflessione condotta da un gruppo

Il lavoro si articola come segue. La sezione seguente descrive la metodologia EFTE impiegata nel condurre lo studio. I risultati vengono poi riportati descrivendo la trasformazione strategica del modello di business sia per le aziende profit che per l'ente pubblico e il terzo settore. Un paragrafo di discussione dei risultati, con particolare riferimento alle organizzazioni del terzo settore, conclude l'articolo.

2. Metodologia

Per lo studio è stato utilizzato un approccio EFTE (estimate, feedback, talk, estimate) (Nelms and Porter, 1985), anche conosciuto come “mini Delphi”. Sono stati raccolti pareri di nove esperti sul tema dei modelli di business durante frangenti complessi, come quello pandemico, provenienti dal mondo accademico ed aziendale. Questa scelta è stata fatta per godere dell'opinione di professionalità multidisciplinari. La provenienza multisettoriale ha permesso di ottenere dei risultati e delle riflessioni valide non solo per le realtà imprenditoriali “classiche” ma anche per le realtà del terzo settore e dell'ente pubblico. Gli esperti sono stati selezionati ed invitati all'interno della rete delle nove università che formano lo SMICT, uno degli otto centri di competenza dell'Industria 4.0 altamente specializzati nati in Italia su iniziativa del Ministero dello Sviluppo Economico (SMICT, 2021). Più precisamente, sono stati individuati volutamente degli esperti con un background multidisciplinare, con specializzazione in sociologia, strategia aziendale, innovazione, ingegneria e processi aziendali, sostenibilità, marketing e comunicazione e politiche pubbliche. L'analisi è stata condotta nei mesi di Marzo e Aprile 2020, durante il primo lockdown generale condotto sul territorio nazionale.

Le indagini e le osservazioni sono state raccolte seguendo fedelmente il percorso descritto da Nelms e Porter (1985); più precisamente:

1. Agli esperti sono state fornite informazioni di base da utilizzare per formulare giudizi;
2. Gli esperti sono stati riuniti e le domande riguardanti le informazioni di base sono state risolte da un responsabile “Delphi”, ricercatore principale dello studio. È stato incoraggiato il confronto tra gli esperti, agevolandoli attraverso strumenti di traduzione della conoscenza (Dal Mas *et al.*, 2020);
3. A ciascun esperto è stato fatto compilare e consegnare un questionario “Delphi”;
4. I risultati del questionario sono stati riassunti e condivisi con l'intero gruppo;
5. I feedback sono stati discussi mantenendo l'anonimato della risposta al sondaggio di ogni individuo;
6. Il processo è terminato attraverso un report riassuntivo dei risultati ottenuti (Bagnoli *et al.*, 2020), poi pubblicato sul web e reso disponibile a tutti.

3. La trasformazione strategica del modello di business

Una trasformazione o innovazione strategica porta alla creazione di un nuovo mercato sviluppando una proposta di valore unica e, quindi, di un nuovo modello di business (Bagnoli *et al.*, 2018, 2019).

Quest'ultimo può essere ottenuto attraverso lo sviluppo di:

- prodotti innovativi (beni e/o servizi), presentati o combinati in modo nuovo, per creare un'esperienza radicalmente diversa nei clienti, coinvolgendoli anche a livello emotivo, intellettuale e/o spirituale;

- processi innovativi per la produzione e/o distribuzione di prodotti esistenti o nuovi che possono portare all'acquisizione di nuovi gruppi di clienti;

- catene del valore innovative, in modo da creare un nuovo spazio di mercato che, rendendo irrilevante la concorrenza, consenta di aumentare il valore sia per l'azienda che per il cliente (Klewitz and Hansen, 2014; Schneider and Spieth, 2013; Teece, 2010).

In termini generali, una delle prime sfide che le aziende devono superare è il classico paradosso tra perseguire una strategia competitiva di differenziazione, aumentare il valore percepito dal cliente e, quindi, il prezzo di vendita del prodotto, o leadership di costo, abbassando il costo di realizzazione del prodotto, facendo leva su un'offerta inferiore, in tutto o in parte, a quella dei concorrenti. Nonostante la ratio diversa che sta alla base, anche il terzo settore e gli enti pubblici possono adottare variegati modelli di business, finalizzati alla soddisfazione dei bisogni dei propri interlocutori (Massaro *et al.*, 2015). Anche per questi interlocutori è fondamentale guardare alla qualità e all'ormai necessaria innovazione del prodotto/servizio offerto.

Una trasformazione strategica richiede di individuare il punto di partenza per la riprogettazione del modello di business, concentrandosi sui punti di forza e di debolezza della realtà analizzata. L'organizzazione dovrebbe identificare le caratteristiche essenziali che distinguono ciascuno degli elementi costitutivi (proposta di valore, fornitori e canali di fornitura, risorse, processi interni ed esterni, prodotti e canali di distribuzione, clienti e società).

A seguito dell'analisi svolta dal gruppo di esperti, la Tabella 1 che segue illustra i 50 paradossi individuati. In particolare, vengono indicati in grassetto quelli maggiormente interessanti per il terzo settore, riportati poi nella discussione.

Tabella 1. Oltre 50 paradossi per ripensare i modelli di business post-pandemia

		FASI	PARADOSSI
1	Paradossi riscontrati durante le varie fasi della crisi	Tutte le fasi	esperienza pratica vs conoscenza teorica
2		Fase 'before' – tempo imperfetto: preparazione alla crisi	predizione/scenarizzazione vs robustezza/antifragilità
3			prevenzione vs assicurazione
4		Fase 'throughout' - tempo presente: tutela dell'operatività nel corso della crisi	difesa dell'esistente vs sperimentazione del nuovo
5		Fase 'after' - tempo futuro: ritorno a una 'nuova' normalità finita la crisi	temporaneo vs permanente
6			continuo vs intermittente
7		Fase 'beyond' – tempo futuro anteriore: trasformazione strategica finita la crisi	ritorno a una 'nuova' normalità vs trasformazione strategica
8			attesa vs azione
9			contingente vs strutturale
10			

11	Paradossi riscontrati all'interno di singoli building block	Società	crescita economica lineare vs crescita economica circolare
12			globalizzazione vs localizzazione
13			libertà/azione privata vs imposizione/intervento pubblico
14			shareholder vs stakeholder
15			condivisione vs esclusività
16			digital transformation vs human touch
17			leadership autoritaria vs empatica
18		fornitori	supply chain corta vs supply chain lunga
19			supply chain concentrata vs supply chain dispersa
20			partnership vs mercato
21		risorse	just in time vs scorte di sicurezza
22			risorse umane vs cyber-physical systems
23			operai interinali vs tecnologi informatici
24			uffici individuali vs infrastrutture informatiche
25			personale locale vs talenti worldwide
26			più cassa e banca vs strumenti di garanzia
27		Processi interni	offshoring vs reshoring
28			lavoro in ufficio vs lavoro da casa
29			celle produttive isolate vs sistemi produttivi humanless
30			sistemi produttivi orientati alla flessibilità efficiente vs sistemi produttivi orientati alla flessibilità ridondante
31			immagine pubblicitaria vs verità rassicurante
32		Processi esterni	eventi offline vs eventi in streaming
33			distribuzione fisica vs e-commerce
34			consegne "a mano" sanificate vs consegne automatizzate
35			servizi offline vs servizi online
36		Prodotti	beni condivisi vs beni personali
37			packaging performante vs packaging sicuro dal punto di vista sanitario
38			materiali autosanificanti vs materiali facili da sanificare
39			sicurezza innovando i beni vs direttive per il loro utilizzo
40			certificazione di qualità vs certificazione sanitaria
41			beni low cost vs beni sostenibili
42			prodotti (per la casa) tradizionali vs prodotti smart
43			prodotti a supporto dell'interazione fisica vs virtuale con persone vs robot
44			mercati Made-in-Italy-push vs mercati Covid-19-pull

45	Clienti e mercati	mercati globali vs mercati locali
46		tradizionali segmenti di mercati vs nuove tribù di consumatori
47		mercato rionale vs marketplace
48		bisogni essenziali vs aspirazioni trascendentali
49		nuove necessità vs nuove abitudini
50	Proposta di valore	Rafforzamento della cultura e dell'identità aziendale vs cambiamento per adeguarsi al contesto

4. Discussione e conclusioni

La crisi a seguito della pandemia da Covid-19 ha un impatto sugli elementi costitutivi del modello di business individuale e sulle relazioni tra tali elementi e, quindi, sull'intero modello con cui diverse organizzazioni lavorano. Emergono dei paradossi che mettono in discussione il modo con cui le organizzazioni, pubbliche e private, profit o non profit, hanno lavorato fino ad oggi. L'individuazione di elementi paradossali vuole fungere da stimolo non solo per le realtà imprenditoriali classiche, ma anche per quelle del terzo settore, che in molti casi sono state profondamente colpite dagli effetti della pandemia e dalle conseguenti restrizioni normative.

Si possono riportare alcuni esempi, particolarmente collegati al terzo settore.

La sospensione temporanea del lavoro in presenza in uffici non essenziali, causata dalla necessità di distanziamento sociale, è stata spesso la spinta per la diffusione del lavoro agile. Questo però a volte non risulta essere efficace come le attività in presenza, soprattutto in alcuni settori come diverse attività facenti parte del terzo settore, ove svolgere attività in presenza risulta essere molto importante per il raggiungimento dei fini istituzionali. Queste realtà dovrebbero capire se la pandemia ha portato ormai all'affermazione definitiva di questa tipologia di approccio o se ci sarà ancora spazio per la condivisione degli spazi lavorativi, e quindi concentrare le proprie forze su un eventuale business model efficace anche a distanza (paradossi n. 7, 10 e 28 tabella n.1). In questo senso, lavorare a distanza potrebbe consentire anche alle aziende no-profit di lavorare con un numero maggiore di soggetti, magari difficilmente raggiungibili fisicamente. L'uso di piattaforme di teleconferenza, workshop online, eventi di formazione o didattica a distanza possono consentire anche alle aziende del terzo settore di promuovere la loro attività in un contesto più ampio e quindi ad un maggior numero di soggetti, riducendo allo stesso tempo i costi di trasporto. Altra riflessione potrebbe essere quella della scelta di organizzare in maniera stabile eventi in streaming, non conoscendo ancora se, quando, e in che termini quelli offline riprenderanno (paradosso n. 32 tabella n.1). Ancora una volta, la dimensione di fatto illimitata del bacino d'utenza online può consentire alle organizzazioni del terzo settore di perseguire i fini istituzionali in misura globale.

Il telelavoro e lo "smartwork" (paradosso 28 tabella n. 1) consente a tutte le aziende di avvalersi di collaboratori senza barriere geografiche. Questo consente da un lato una maggiore soddisfazione del lavoratore (si pensi a chi deve gestire situazioni familiari delicate, o a chi in condizioni normali deve trascorrere molto tempo in auto o nei mezzi pubblici per recarsi nel luogo di lavoro), dall'altro la possibilità di attrarre "talenti" che, in condizioni di lavoro

d'ufficio, non sarebbero disponibili in quanto geograficamente lontani. Questa possibilità può risultare particolarmente interessante anche per l'ente pubblico, da sempre in cerca dei migliori collaboratori, e il terzo settore, che quindi potrebbe reclutare volontari e addetti per alcune funzioni senza alcuna barriera geografica.

Un altro aspetto rilevante è connesso alla spinta dello sviluppo dell'e-commerce. L'esperienza fisica di acquisto è sicuramente diversa da quella online, questo ultimo più immediato, con spettro di scelta più ampio, ma più "freddo", privo di un confronto umano (paradosso n.33 e 47 tabella n.1). Come moltissime realtà, anche quelle del terzo settore dovrebbero pensare se la pandemia ha portato all'affermazione definitiva dell'e-commerce e della consegna a domicilio o se l'esperienza fisica tornerà a svilupparsi.

La grande sfida è quindi mappare e comprendere gli elementi costitutivi più colpiti, riconoscere i potenziali paradossi suggeriti dalla crisi e ripensare le scelte strategiche di compromesso tra i poli, i bisogni e gli interessi opposti. I paradossi difficilmente possono essere "risolti". Tuttavia, tutte le organizzazioni, pubbliche e private, profit e non profit dovrebbero cercare di cogliere la crisi pandemica quale occasione per innovare il proprio modello di business.

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Foreign direct investment, institutional development, financial development and economic growth

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Abstract

The aim of this paper is to focus on relationship between FDI, financial development, institutional development and economic growth in North African countries from 1995 to 2017. Using the system Generalized Method of Moments (GMM) in a panel data analysis, we justify the positive effect of FDI, institutional development and financial development on the economic growth in North African countries. We also noted the important complement between FDI, institutional development and financial development.

Keywords: Foreign direct investment, Institutional development, Financial development, economic growth, Panel data analysis

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1.Introduction

From an endogenous growth perspective, economic growth is determined by accumulation of human capital Romer (1986, 1990), institutional development North (1970, 1991), capital flows Findlay (1978), research and development, economic stability, innovation, financial development Mackinnon (1973) and Show (1973), etc.

FDI contributes to economic growth through several transmission channels as intensification international trade through the creation of dynamic comparative advantages, technology transfer and accumulation of human capital. These three benefits are often not known as spillovers. In addition, there are other channels of connection between FDI and economic growth such as capital formation, good management within new enterprises and intensification competitive sphere.

Institutional development contributes directly or indirectly to economic growth. North (1991) defines the term institutional as all informal constraints such as sanctions, taboos, customs,

traditions and codes of conduct, and formal rules such as constitutions, laws and private property rights.

The term quality of institutions includes the index of economic freedom. In this regard, according to the Fraser Institute (2018), institutions contains size of government, legal system and respect for private property rights, monetary stability, degree of commercial freedom and regulation.

Financial development affects economic growth through the mobilization of savings Mackinnon (1973) and Show (1973). Indeed, following the liberalization of the interest rate, mobilization of savings facilitates the financing of agents financing needs. Again, financial development effectively allocates and mobilizes external resources. That is, businesses in developing countries are financed from international financial institutions. This operation will make it possible to mobilize global savings. This operation will make it possible to mobilize global savings.

The organization of the paper is as follows: The first section presents the effect of FDI and determinants of economic growth according to theoretical reviews. The second section deals with date and econometric specification. The third section deals with the presentation of the results obtained.

2. Review of literature

The economic benefits of attracting FDI are generally different. The latter derives from the effects of technology transfer, encouragement of exports, improvement of domestic investment, intensification of the competitive edge, and good management within new firms in the event of mergers and acquisitions.

Regarding technology transfer, Khun (2018) justified the positive and significant impact of FDI on economic growth in Cambodia over the 2006-2016. This effect is explained by the transfer of new technologies to physical capital and absorption, the diffusion of new knowledge of human capital.

Mohamed (2016) showed that FDI only positively affects Moroccan growth from 1980 to 2012 that FDI is concentrated in the industrial sector and of French origin. It explained this condition by the existence of technologies in the sector in which FDI is concentrated. However, the technologies that accompany FDI are disseminated to physical capital.

In theory, effect of FDI on economic growth depends on financial development of the host countries. In this regard, Mohamed Sghaier (2018) focuses on the relationship between FDI, financial development and economic growth in North African countries from 1992 to 2016.

The use of the GMM econometric technique on panel data shows the positive and significant effect of FDI and financial development on GDP. It showed that the impact of FDI on economic growth in the North African region depends on the level of financial development. That is, the more financial system is developed, the greater the effect of FDI on GDP.

The trade openness of the host countries facilitates export and import processes of foreign companies products. In this perspective, Diouf and Hai (2017) focus on the relationship between FDI, trade openness and economic growth in 13 West African countries from 1980 to 2015. The results of the weighted ordinary least squares justify positive effect of FDI, trade openness on economic growth. The study indicated that there is a one-way causality between FDI and economic growth and a two-way causality between trade and economic growth. According to Diouf and Hai (2017), impact of FDI on GDP depends on the degree of trade openness.

The attractiveness of FDI is not only due to financial development, human development, commercial openness, but depends on the development of institutions. These guarantee the private ownership of foreign investors. Still, democracy and good governance in host countries can attract the sight and attention of foreign investors.

Malikane and Chitambara (2017) examined the link between FDI, democracy and GDP in 30 countries in southern Africa. They justify that FDI and democracy positively affect economic growth, so effect of FDI depends on degree of democracy

Hammami and Chakroun (2009) analysed the link between the quality of institutions, economic, social performance and attractiveness of long-term FDI through the use of cross-sectional data for 145 countries. They showed the significant correlation between quality institutional and attractiveness of FDI.

Amadou (2018) analysed the effects of the interaction between inflation volatility and governance quality on FDI in 34 countries in sub-Saharan Africa from 1996 to 2014. It has shown that inflation volatility negatively affects attractiveness of FDI, while improving the quality of governance reduces negative impact of inflation volatility on the attractiveness of FDI.

Mihaela et al. (2018) examined the relationship between quality institutional and attractiveness of FDI in 110 countries (41 developed and 69 developing and poor countries) from 2002 to 2012. Regression using the ordinary least square method shows that the government of developed countries has a positive and significant effect on the attractiveness of FDI. The relationship between good governance and FDI is explained by political stability, the

application of legal rules and respect for citizens' private property rights. They showed that size of government in developing and poor countries has a positive and significant effect on FDI.

Azmat (2007) tested the link between governance and FDI in a sample of Asian and Latin American countries from 1996 to 2002. Econometric technique of MCO regression shows that there is a positive and significant relationship at the 1% threshold between rule of law, regulation, government efficiency and political stability. Corruption control has a positive and significant effect at the 5% threshold on attractiveness of FDI.

According to previous reviews by Khun (2018), Mohamed Sghaier (2018), Diouf and Hai (2017), Hammami and Chakroun (2009) and Amadou (2018) and Mihaela et al. (2018), we see the effect of FDI on the economic growth of host countries depends on financial development and institutional development, trade openness and human development.

3. Data and Empirical methodology

3.1 Data

We study processes data from the 4 North African countries: Tunisia, Egypt, Algeria and Morocco from 1995 to 2017. The per capita GDP growth rate (constant USD 2010) refers to dependent variable. FDI, institutional development, financial development are independent variables, the other variables are control variables. The data base obtained from the World Bank (2018).

- FDI refers to the net investment entry to acquire a sustainable management interest (10% or more of the voting shares) in an enterprise operating in an economy other than the investor's. This is sum of own funds, reinvestment of profits, other long-term capital and short-term capital as shown in the balance of payments. The expected sign of FDI is positive.
- Institutional development is measured by the Economic Freedom indicator. This indicator contains private property law, international trade, size of government, regulation, corruption control and legal system. Each sub-index contains other sub-indices. In total, the economic freedom index contains 42 distinct variables. Each sub-index scores between 0 and 10. The Economic Freedom indicator series is obtained by the Fraser Institute (2018). The expected sign of the coefficient of institutional development is positive.
- Financial development can measure by the ratio M2 as a percentage of GDP, ratio of domestic credit distributed by the banking sector as a percentage of GDP, ratio of domestic credit distributed to the private sector and GDP. We measured financial

development by ratio of domestic credits to the private sector as a percentage of GDP because the financial systems that collect deposits and then direct credits to government or state-owned enterprises.

- Gross fixed capital formation is measured by value of domestic investment and stock of capital as a percentage of GDP. Barro (1999), Balasubramanyam and al. (1996) have justified the positive use of domestic investment for economic growth.
- Inflation is measured by the general increase in consumer prices. The expected sign of inflation coefficient is negative. High inflation can hamper purchasing power, consumption and subsequently demand and economic growth.
- Human development can measure by the rate of primary, secondary or university enrolment, number of branches in higher education, demographic rate. Generally, human development positively affects economic growth (Han and Lee (2020)). Due to the absence of the secondary and university enrolment rate database in our study, we used primary enrolment rate as a proxy for human development.

3.2 Methodology

Relative to time series, dynamic panel data holds one or more delays of the independent variable appear as dependent variables in model. Because of the complexity of the econometric model in the form of dynamic panel data (the existence of a dependent variable to right of independent variable) standard econometric estimation techniques do not allow to obtain unbiased estimates. Econometric technique GMM allows econometrics to simplify indignity of variables essential in case of presence of one or more delays of variable to explain appear as explanatory variables. It also allows controlling specific effects. Panel data estimation by econometric GMM technique born by Arrelando and Bond (1991), Arrelando and Bover(1995) The objective of our study is to identify complement between FDI and institutional development, financial development and economic growth in North African countries. Specificity of models below is inspired by Choong (2012).

$$\Delta GDP_{it} = \alpha_0 + \alpha_1 \Delta GDP_{it-1} + \alpha_2 FDI_{it} + \alpha_3 FD_{it} + \alpha_4 HD_{it} + \alpha_5 INF_{it} + \alpha_6 ID_{it} + \alpha_7 GFCF_{it} + \alpha_8 FD.FDI_{it} + \varepsilon_{it}$$

With:

$$\varepsilon_{it} = \gamma_i + \mu_t + \theta_{it}$$

$$t = 1995 \dots 2017 \text{ et } i = 1, 2, 3, 4$$

To identify role of financial development in improving economic growth through FDI we have estimated model below.

$$\Delta GDP_{it} = \alpha_0 + \alpha_1 \Delta GDP_{it-1} + \alpha_2 FDI_{it} + \alpha_3 FD_{it} + \alpha_4 HD_{it} + \alpha_5 INF_{it} + \alpha_6 ID_{it} + \alpha_7 GFCF_{it} + \alpha_8 FD.FDI_{it} + \varepsilon_{it}$$

To identify role of institutional development in improving economic growth through FDI we have estimated following model.

$$\Delta GDP_{it} = \alpha_0 + \alpha_1 \Delta GDP_{it-1} + \alpha_2 FDI_{it} + \alpha_3 FD_{it} + \alpha_4 HD_{it} + \alpha_5 INF_{it} + \alpha_6 ID + \alpha_7 GFCF_{it} + \alpha_8 ID.FDI_{it} + \varepsilon_{it}$$

- **Unit root test**

The IPS approach has several advantages over the Levin, Lin and Shin test by taking into account the heterogeneity of autoregressive root under the alternative. Im, Pesaran and Shin (2003) propose a test statistic based on average of the individual DF and ADF statistic. The Im, Pesaran and Shin (2003) tests are ranked among first generation stationary tests. The table below summarizes unit root test of the different series.

Table 1 Stationarity Test

Im, Pesaran and Shin			
variables	Level	1st difference	2nd difference
GDP	0.056	-1.270	-6.801
	0.522	0.101	0.000
FD	1.490	-1.447	-6529
	0.931	0.073	0.000
FDI	-0.023	-0.738	-4.523
	0.490	0.230	0.000
ID	-2.823	-7.968	-10.726
	0.002	0.000	0.000
INF	2.682	3.802	-7.405
	0.996	0.000	0.000
GFCF	2.439	2.240	-6.198
	0.992	0.012	0.000

Source : Author STATA 15

The table above does not reject the null assumption of a unit root at level of GDP, gross fixed capital formation, financial development, inflation and FDI. That is, GDP, gross fixed capital formation, financial development, inflation and FDI are not flat at the level. However, index of institutional development is stationary. When we go to 1st difference we notice that all variables become stationary except GDP and FDI. In the second difference all the variables become stationary. In this case, we accept that variables are co integrated of order 2.

- **Serial autocorrelation test**

The serial autocorrelation test is used to test an error autocorrelation greater than unit. Autocorrelation test, also known as the Breusch-Godfred test (1980). Serial autocorrelation test is based on a search for a significant relationship between residues and same shifted residue. Breusch-Godfred (1980) hypothesis is formulated as:

H0: Lack of autocorrelation

H1: Autocorrelation

The decision is taken by classical Fischer test of nullity of coefficients or by the distributed LM statistic according to a Khi-2 law at p degrees of freedom.

With: $LM = T \times R^2$

If $LM > \chi_p^2$ read, error independence hypothesis is rejected. Table below displays the error independence test results.

Table 2 Breusch-Godfred LM serial autocorrelation test

Test	Breusch-Godfred test		
Models	Model 1	Model 2	Model 3
χ^2	26.093	23.625	18.553
P. χ^2	0.000	0.000	0.000

Source : Author STATA 15

According to results of Breusch-Pagan LM test the null hypothesis of independence of errors is rejected. That is, there is a serial autocorrelation problem for the 3 models.

- **Individual heteroscedasticity test**

In econometric terms, heteroscedasticity is said if variances of the residuals of variables are different. homoscedasticity correspond to case where residues of variables are constant. Most commonly used test for heteroscedasticity is Wald test (2000). Null hypothesis of Wald test assumes homoscedasticity. So heteroscedasticity test problem is this:

H0: Homoscedasticity

H1: heteroscedasticity

If probability associated with test is less than 5% H0 is rejected. If probability is greater than 5%, then null hypothesis is verified. Table below displays the results of Wald test.

Table 3 Wald test

Test	Wald test		
Models	Model 1	Model 2	Model 3
χ^2	35.78	22.90	42.06
P. χ^2	0.000	0.001	0.000

Source : Author STATA 15

Based on this table, we reject homoscedasticity hypothesis and assume heteroscedasticity hypothesis in most models.

4. Empirical results

After processing data on STATA 15 the following results are obtained. Table below shows the results of GMM estimate.

Table 4 Estimation table

<i>Variable</i>	<i>Model 1</i>	<i>Model 2</i>	<i>Model 3</i>
<i>Constant</i>	0.041765 (***)	0.083432 (***)	0.100947 (**)
<i>Initial GDP per capita</i>	-0.089259 (*)	-0.085374 (*)	-0.005374 (***)
<i>Foreign Direct Investment</i>	0.009827 (**)	0.011721 (***)	0.009974 (**)
<i>Financial Development</i>	0.048065 (*)	0.052194 (**)	0.042021 (***)
<i>Inflation</i>	-0.050976 (***)	-0.042229 (***)	-0.066121 (**)
<i>Institutional Development</i>	0.032203 (**)	0.049546 (**)	0.041965 (*)
<i>Human Development</i>	0.049409 (***)	0.066662 (***)	0.062922 (*)
<i>Gross fixed capital formation</i>	0.061573 (n.s)	0.068059 (n.s)	0.17239 (**)
<i>Foreign Direct Investment* Financial Development</i>	-	0.005496 (*)	-
<i>Foreign Direct Investment* Institutional Development</i>	-	-	0.065223 (*)
<i>Probabiliy Sargan test</i>	0.070159	0.078791	0.070684

T-Statistics are in parentheses. Significance levels at which the null hypothesis is rejected: *** 1%; ** 5%, and * 10%.

Source: Author STATA 15

Sign associated with FDI is positive and statistically significant at 5% level. This is contribution of FDI inflows to economic growth of North African countries. Our result is corroborated with studies of Diouf and Hai (2016) and Khun (2018). Positive relationship between FDI and economic growth is explained by FDI inflow to region leading to transfer of new technologies which improves physical productivity which is a source in economic growth. Sign associated with variable “institutional development” is positive and statistically significant at 5% level. That is, development institutional positively affects economic growth in North African countries. Our research result is consistent study Mihaela and al. (2018). From an economic point of view, relationship is explained by good governance, respect for private property rights, compliance with legal rules can encourage the view of foreign investors. Financial development has a positive and statistically significant effect on economic growth in North African countries. According result, it is said that financial system in North African countries from 1995 to 2017 is developed. This result is contradicted by traditional literature by Rostami and al. (2017). Our result can be explained by the agreement of loans granted to the private sector in the North African region by removal of credit ceilings and reduction of compulsory reserves of commercial banks at central bank.

As regards control variables, the positive effect of human capital on economic growth is justified. That is to say, human development in North African countries has a positive and significant effect. This relationship is explained by quality of workforce in North African countries following the improvement of the education system and the completion of training cycles. Our result is consistent with study by Alexander and al. (2019).

The general increase in prices has a negative and statistically significant effect on economic growth at 1% level. This is explained by effect of rapid increase in prices in region on purchasing power and subsequently in aggregate demand which weakens economic growth.

The sign associated with gross fixed capital formation is positive and statistically insignificant. Lack of allocation of gross fixed capital formation to economic growth in North African countries is explained by high burden of officials and investment in non-productive sectors, which threatens economic performance in long term.

The delayed variable has a negative effect on dependent variable. Link between the two is explained by assumption of convergence in countries towards the same point of GDP per capita in the long term. Our result is consistent with work Sala-i-Martin (1997).

In a second step we estimate interaction effect between FDI and financial development on economic growth in North African countries. We observe positive and significant effect of FDI*FD variable on economic growth and improvement of financial development effect and FDI. The improvement in FDI coefficients and financial development is explained by financial development in North African countries attracting FDI. It effectively mobilizes and allocates external resources, which facilitates financing of companies located in North Africa region.

In a third step we estimate interaction effect between FDI and institutional development on economic growth. We noted that FDI*institutional development variable has a positive and statistically significant effect at 10% level. Again, increase in growth effect of FDI has been observed. This improvement is explained by important role institutions in economic growth through the attractiveness of FDI. In this case, it can be seen that more liberal countries can benefit more from effects FDI.

5. Conclusion

Our study focuses on the relationship between FDI and growth in presence of financial development and institutional development. Our research results are consistent with teaching of our theoretical analysis.

Using the system Generalized Method of Moments on panel data from 4 North African countries from 1995 to 2017 justifies contribution FDI, institutions and financial development

and human development for economic growth. However, gross fixed capital formation does not affect economic growth in North African countries. The general increase in prices handicaps GDP in North African countries.

We tested effect of complement between financial development and FDI on economic growth. We have seen important role of financial development in North African countries in effect of FDI on economic growth. We have explained this relationship through financial development strategy in North African countries in attractiveness FDI.

We examined interaction effect between economic freedom as an index institutional development and FDI on economic growth. We have seen positive effect of complement between FDI and institutional development. This relationship is explained by development of institutions in North African countries with respect for private property rights of foreign investors.

In light of our results and explanations, we urge North African countries to further develop the financial system to benefit more from effects FDI on economic growth. Again, we recommend North African countries to develop institutions to attract more FDI. But the question now is, does FDI persist in regional income inequality?

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International tourism, growth and environmental quality: the case of three North African countries

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Abstract: This paper examines the interactive relationships between international tourism, economic growth and environmental quality in three countries of North Africa (Tunisia, Maroc, Egypt) over the period 1981 -2019. The study used the ARDL model. The results show that tourism has a direct and statistically significant impact on the level of carbon dioxide) emissions (CO₂) and economic growth in the long run. The results also confirm the existence of an inverted U-shaped relationship for Morocco and Egypt between CO₂ emissions and income level, while this relationship takes the form of a U- shaped in Tunisia. The error correction models in this study have shown that: (1) CO₂ emissions converge towards their long-term equilibrium situation with a speed of the order of 5.8% in Morocco, 20% in Egypt and 27.9% in Tunisia through economic growth channels, of the consumption of energy and tourism. This finding reveals that the growth of tourism allows significantly, climate change to move to higher levels. (2) economic growth converges towards its long-term equilibrium by an adjustment speed of the order of 25.7% in Morocco, 5.8% in Egypt and 2.1% in Tunisia.

Keywords: International tourism; Environmental quality; Economic growth; Energy consumption; ARDL model.

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1.Introduction

Over the past three decades, the study of environmental quality has taken on a major concern in numerous attempts in the environmental economics literature to shed light on the main factors that can affect the quality of the environment. environment. The CO₂ emissions used in the literature as a proxy for measuring climate change are of primary concern to both developing and developed countries. Of particular interest to this debate is the study of the Environmental Kuznets Curve (CEK), which predicts that the quality of the environment deteriorates with economic development at low-income levels but improves with development. economic at high income levels. In this perspective the pioneering work goes back to Grossman and Krueger (1991) who concluded that air pollution increases in the early stages of growth with the level of income, but once the GDP per capita reaches a certain threshold value the relation overturns. This relationship in the form of an inverted U is later justified by various works (Selden and Song 1994, Holtz-Eakin and selden 1995; Dinda S. 2004; Luzzati, T. and Orsini, M. 2009; Costantini, V. and Martini, C. 2010; Fodha, M., & Zaghoud, O., 2010).

The relationship between growth and environmental quality developed further by introducing other variables other than the level of GDP and the pollutant. This multivariate

framework has facilitated the elucidation of both how these factors contribute to environmental degradation and whether the CKE hypothesis still survives after controlling for these relevant variables. Frequently used variables are energy consumption, international trade, urbanization. The inclusion of energy consumption in the study of environmental conditions is an obvious choice, given its impacts on the generation of pollution. Indeed, energy consumption is considered as the main source of pollution and environmental degradation in various empirical works (Ang 2008; Soytaş and Sari 2009; Apergis and Payne 2010; Arouri, Ben Youssef, Me Henni and Rault, 2012). A side of the power consumption, trade openness is also seen as a factor determining the quality of the environment, however, its impact is generally less clear. The ambiguity of the impact of trade on the quality of the environment is well reflected in the literature. Indeed, some studies have concluded that trade negatively affects the quality of the environment (Ang, 2009; Jalil and Feridun, 2011; Nasir and Rehman, 2011); others have verified the opposite hypothesis which predicts a positive effect (Birdsall and Wheeler, 1993; Ferrantino, 1997; Grether et al., 2007); while for others, trade negatively affects the quality of the environment in the long term based on ARDL models (Jalil and Mahmoud, 2009; and Javanthakumaran et al., 2012).

In the same perspective, urbanization is taken as a factor influencing the quality of the environment. Results of previous studies have shown mixed effects on environmental conditions. On the one hand, a high level of the urbanization rate increases the quantities of pollutant emitted due to industrial concentration and congestion in urban areas (Panayotou, 1997). On the other hand, urbanization can have a positive effect on environmental quality due to the economies of scale of emission reduction technology in urban areas compared to rural areas (Torrás and Boyce, 1998). All the more, this is more conducive to mobilizing the efforts of people in urban areas to influence environmental protection policies (Rivera-Batiz, 2002; Farzin and Bond, 2006). Meanwhile, the role of urbanization turned out to be insignificant in the study by Qu and Zhang (2011).

However, and despite taking into account various factors that can influence growth and the quality of the environment, a few sectors or variables deserve to be studied. From such a perspective, the tourism sector can present a field of study. In this sense, tourism today presents one of the largest and most dynamic industries in the world. Thus, the international tourism revenue in 2012 reached a total of 1,075 billion dollars generated by 1,035,000,000 international tourist arrivals (UNWTO, 2013). Also world tourism participates in the creation of 1 to 11 jobs and generates 9% loan of the global gross domestic product (GDP) (World Tourism and Travel Council - WTTC, 2013). In this regard, any increase in the number of international tourists not only generates economic growth but requires the consumption of additional amounts of energy (Liu J., Feng T., Yang X., 2011). However, the development of tourism is also likely to bring changes to the climate. Thus, increased tourism activities may contribute to increased energy demand within various functions, such as transport, catering, accommodation and management of tourist attractions (Becken S. et al., 2003; Becken S et al. 2003); Becken S et al. (2001), Gössling S. (2002). This is also likely to lead to environmental degradation and pollution. The consideration of the tourism sector as a source of pollution is well confirmed with the World Summit on Sustainable Development in 2002 in Johannesburg which recognized by international tourism as one of the important consumers of energy (Nepal; 2008).

In this study we intend to make two contributions. First, we looked at the effect of tourism on growth and environmental quality in the North African region. Secondly, we tried to fill r the

deficiency relating to the verification of the hypothesis of the environmental Kuznets curve in the region.

To take these contributions listed above, we chose the a next step; after demonstrating the importance of the subject, a second section will be devoted to an e briefly reviewed e literature on tourism relationship, growth and quality of environment. The third section will describe the data and methodology used to explore the effect of tourism on the environment and growth. Then, the main results obtained as well as their interpretations will be illustrated in the fourth section . Finally, we will end with the conclusion and the different political implications.

2.Literature

In recent years, environmental issues have been of concern to economists and politicians. In general, the taking into account of the quality of the environment and the analysis of the links between energy consumption, economic growth and CO₂ emissions has been dealt with under various research axes. Some studies have analyzed the relationship between energy consumption and economic growth (Odhiambo N . M .,2009; Abosedra S . Et al., 2009); Stern, D., 2011; Fuinhas, JA and Marques, AC, 2011). This work has verified the role of energy in the contribution of economic growth. Some studies have analyzed the relationship between income level and CO₂ emissions through the Kuznets environmental curve (Dinda S., 2004; Luzzati, T. and Orsini, M., 2009; Costantini, V. and Martini, C., 2010; Fodha, M., & Zaghoud, O. (2010). Other studies have analyzed the joint relationship between energy , growth and pollution (Zhang XP, Chen XM, 2009; Arouri, MH et al., 2012; Sbia, R. et al., 2014).

The issues related to the tourism sector who knows nowadays a remarkable development, are increasingly the attention of economists and of contemporary researchers . Indeed, an increase in tourism activities comes with increased demand for energy within various functions: the importance of energy for the tourism sector is undeniable. Thus, the increase in energy consumption due to the development of tourism can have a negative impact on the quality of the environment. It is obvious that environmental degradation is also likely to occur due to the development of tourism through the construction of hotels and other tourist establishments to the detriment of green spaces and also through additional energy consumption. The growth literature has indicated that most tourism activities contribute to environmental pressure (Day, J., & Cai, L. P, 2012; Duffy, 2001).

Faced with the environmental challenges of tourism, a bit of literature has developed to analyze the effects of tourism on the quality of the environment and climate change. Some studies have looked for the implications of tourism with regard to environmental issues, such as its contribution to greenhouse gas emissions and global warming (Becken S et al. 2003 ; Gössling S. 2002 ; Becken S. 2005 ; Bode S et al. 2003, Nielsen et al. 2010 , Simpson et al., 2008). Some studies have focused on the tourism-energy consumption relationship (Tabatchnaia-Tamirisa N et al., 1997 ; Gössling S 2000; Becken S, Simmons DG, 2002) ; other studies have looked for the effect of the tourism industry on the quality of the environment (Xuchao et al., 2010; Hsin -Jung Hsieh and Shiann -Far Kung, 2013; Jun Liu et al., 2011). So, from the above, we can conclude the effect of the tourism sector in the phenomenon of climate change. Recent literature confirms this finding.

In this sense, Katircioğlu (2015) studied the effects of tourism growth on climate change in the case of Turkey. He found that tourism affects growth not only through a huge increase in energy consumption but also through huge increases in climate change. Referring to data from Cyprus, a tourist destination island in the Mediterranean, Katircioğlu et al. (2010) analyzed the effects

of tourism growth on energy consumption and climate change. Their conclusion confirms that the development of tourism is a catalyst for increasing carbon emissions and energy consumption. Lee and Brahmairene (2013) used data from the European Union (EU) to study the influence of tourism on economic growth and CO₂ emissions using econometric panel data procedures. They noticed that tourism has a negative and significant impact on the increase in CO₂ emissions (Secinaro et al., 2020).

Salih Turan Katircioğlu (2014) examined the relationship between tourism development and carbon emissions in Singapore through environmental Kuznets curve hypothesis testing. The results show that carbon emissions and tourism development are in long-term equilibrium relationship. The CO₂ emissions converge towards its long-term equilibrium level with an adjustment speed of 76.0%. The findings confirm that tourist arrivals have a negative and significant effect on carbon dioxide emission levels both in the short term and in the long term.

Zaman et al. (2016) examined the relationship between economic growth and CO₂ emissions, the development of tourism, domestic investments and health spending in a group of three diverse regions of the world, including Asia Orientale and u Pacific Union E uropean and countries of high income OECD countries and non-OECD on the period 2005-2013 . Their empirical work yielded different results, in particular , i) tourism is determined by economic growth, domestic investment and health spending , ii) tourism and energy induce environmental degradation .

The harmful effect of tourism on the quality of the environment is also confirmed by Saenz - de- Miera and Rossello (2014). In fact, the authors emphasized the negative externality of tourism activities, which leads to climate change and air pollution. The results of their analysis s empirical s also show that the number of tourist arrivals is not the only contributor to increased emissions of carbon dioxide in the atmosphere, but also the pressure of the resident population in Spain a determinant of PM10 emissions in the country. Omri, Shahbaz , Chaibi and R ault (2015) , examined the long-term relationship between tourism, environmental quality, energy consumption, political instability and economic growth in the countries of the region MENA . Their conclusion is that the number of arrival s international tourists is increasing r significant economic growth so that proved the hypothesis which states that economic growth is determined e by tourism in the region.

The previous discussions e s confirmed connections on the nature of the relationship between tourism, economic growth, environmental quality and energy consumption and also on the verification of the hypothesis of the Environmental Kuznets Curve worldwide. This study investigates the relationship between the level of GDP per capita, air pollution, tourist arrivals and energy consumption, in order to determine the effect of tourism on the quality of the environment and the legitimacy of the hypothesis of the environmental Kuznets curve (EKC) in the three countries of North Africa. These findings would help to present sound policy implications for environmental sustainability in the region.

3.Data, econometric model and methodology

3.1. Data

The data used in this document is collected from the development indicators of the World Bank (WDI) and the World Tourism Organization (UNWTO). The do fro m cover the 1981-2019 period . The variables used in our study are the number of international tourism arrivals in

logarithm (LNTOURI), gross domestic product per capita in logarithm (LNGDP), energy consumption per capita in logarithm (LNEC) and CO emissions. 2 per capita in logarithm (LNCO2). Our data relate to a sample of three North African countries namely Tunisia, Morocco and Egypt.

3.2. Econometric Model:

In our study, the starting point of the theoretical analysis is to consider international tourist arrivals as a determinant of growth and CO2 emissions. Our presentation will use the model used by Katircioglu et al. (2014). Thus, the following "tourism-induced" functional relationships will be used in this study.

$$CO2_t = f(GDP_t, GDP_t^2, EC_t, TR_t) \quad (1)$$

$$GDP_t = f(EC_t, CO2_t, TR_t) \quad (2)$$

These functional relationships in equation (1,2) can be expressed in logarithmic form to capture the elasticities of our variables in the long term period (Katircioglu, 2010) :

$$\ln CO_{2t} = \beta_0 + \beta_1 \ln GDP_t + \beta_2 \ln GDP_t^2 + \beta_3 \ln EC_t + \beta_4 \ln TOURI_t + \varepsilon_t \quad (3)$$

$$\ln GDP = \alpha_0 + \alpha_1 \ln EC_t + \alpha_2 \ln CO_{2t} + \alpha_3 \ln TOURI_t + \varphi_t \quad (4)$$

Where t is the period of time, lnCO2 is the logarithm of CO2 emissions, lnGDP is the logarithm of the level of GDP, lnEC is the logarithm of the energy used and lnTOURI is the logarithm of the number of international tourist arrivals.

However, the use of the dependent variable in equations (1) and (2) at their long-term equilibrium levels may not be immediately following a change in one of its determinants. Thus, the speed of adjustment between the short and the long term of the levels of the dependent variables can be captured by estimating the following error correction model:

$$\Delta \ln CO_{2t} = b_0 + \sum_{i=1}^n b_1 \Delta \ln GDP_{t-i} + \sum_{i=1}^n b_2 \Delta \ln GDP_{t-i}^2 + \sum_{i=1}^n b_3 \Delta \ln EC_{t-i} + \sum_{i=1}^n b_4 \Delta \ln TOURI_{t-i} + \gamma_5 \varepsilon_{t-1} + \mu_t \quad (5)$$

$$\Delta \ln GDP = \alpha_0 + \sum_{i=1}^n b_1 \Delta \ln EC_{t-i} + \sum_{i=1}^n b_2 \Delta \ln CO_{2t-i} + \sum_{i=1}^n b_3 \Delta \ln TOURI_{t-i} + \theta_4 \varphi_{t-1} + \zeta_t \quad (6)$$

Where Δ represents the first difference operator , and respectively represent the error correction terms (ECT) of the two models. The (ECT) in both equations show the speed of the adjustment of the imbalance between the short and the long term of the dependent variable. We expect that the (ECT) will have a negative and significant sign (Gujarati DN. 2003).

3.3. Methodology

To study the long-term relationship between the variables, the Autoregressive Dynamic Lagging (ARDL) method is used in our study. The ARDL cointegration technique is introduced by Pesaran and Shin (1999) and Pesaran et al. (2001). Thus according to Pesaran et al. (2001), the use of the model jump test (ARDL) is more advantageous than other cointegration techniques based on the tests of Engle and Granger (1987), Johansen (1991) and Johansen and Juselius (1990). The first advantage is that this approach is applicable even if the explanatory variables are perfectly I (0), perfectly I (1) or mutually co-integrated. This method does not require that the series be integrated of the same order to find a possible cointegrating relationship between these variables. The second advantage is that this method has better statistical properties in small samples. The estimators derived from the Johansen and Juselius approach are not robust when the studied sample is small, as in this study. In addition, Pesaran and Shin (1999) show that using an ARDL model, the ordinary least squares estimators of the short-run parameters are ϕ -consistent and the estimators of the long-term coefficients of the ARDL model are super-consistent in small samples (Narayan and Peng, 2007).

So, before we apply this test, we determine the order of integration of all variables using unit root tests. The aim is to ensure that the variables are not I (2) in order to avoid spurious results. In the presence of integrated variables of order two, we cannot interpret the values of the F statistic provided by Pesaran et al. (2001).

4. Results and discussions

Our study uses the Dickey-Fuller (ADF) and Phillips-Perron (PP) tests to analyze the stationarity and integration levels of our variables. Table 1 presents the results of the ADF and PP unit root test in level and in first difference for the study variables. Our results show that all the variables are non-stationary in level for the three countries of our study, namely Morocco (panel A) Egypt (panel B) and Tunisia (panel C). However, the stationarity of our variables is well justified in the three countries in first difference. Hence we can use the ARDL approach and the application of the jump test to study the long term relationship between growth, environmental quality, tourism and energy consumption is quite valid.

Table 1 : stationarity of variables

Variable s	panel A (Morocco)				panel B (Egypt)				panel C (Tunisia)			
	ADF Test		PP Test		ADF Test		PP Test		ADF Test		PP Test	
	In level	First difference	In level	First difference	In level	First difference	In level	First difference	In level	First difference	In level	First difference
LN (TR)	-1.52 [9]	-6.51 [7] ***	-1.56 [7]	-4.88 [11] ***	-0.72 [9]	-3.61 [8] ***	-0.8 [10]	-6.96 [38] ***	-0.72 [9]	-3.61 [8] ***	-0.8 [10]	-6.96 [38] ***
LN (CO2)	-0.22 [9]	-3.62 [8] ***	0.37 [2]	-6.01 [22] ***	-0.24 [9]	-3.6 [8] ***	-1.09 [10]	-9.02 [18] ***	-1.9 [9]	-3.43 [8] ***	-0.65 [20]	-9.76 [82] ***
LN (EC)	1.24 [9]	-3.43 [8] ***	1.83 [2]	-6.02 [25] ***	-0.82 [9]	-3.62 [12] ***	-2.56 [6]	-5.67 [18] ***	-1.09 [13]	-2.9 [12] **	-1.06 [22]	-7.02 [61] ***
L (NGDP)	-0.44 [13]	-7.37 [4] ***	1.13 [42]	-8.1 [37] ***	-1.44 [5]	-3.10 [4] ***	-0.89 [7]	-5.12 [9] ***	0.11 [9]	-3.14 [8] ***	0.61 [1]	-6.19 [20] ***
LN (GDP) 2	-0.33 [13]	-7.32 [11] ***	1.35 [44]	-7.93 [37] ***	-1.32 [5]	-3.02 [4] ***	-0.72 [8]	-5.06 [9] ***	0.18 [9]	-3.08 [8] ***	0.75 [1]	-6.1 [20] ***

SC is used, selecting the optimal number of lags for ADF testing, while “ Bandwidth ” is used for PP testing. Critical values related to ADF and PP tests were provided by MacKinnon (1996). The numbers in square brackets represent the number of auto-selected lag using the “ Bartlett kernel . ” Note that only the constant is included in the tests. (** *), (**) and (*) indicate statistical significance at 1%, 5% and 10% respectively

To study the long-term relationship between the variables of our study, the Bonds cointegration test is used in an autoregressive dynamic delay modeling (ARDL). This approach was developed by Pesaran et al. (2001) and can be applied whatever is the integration variable order (regardless of what the variables are purely I (0), I (1) or mutually co -Integrated). The use of the ARDL model involves estimating the following error correction models:

$$\Delta \ln CO_{2t} = b_0 + \sum_{i=1}^n b_1 \Delta \ln GDP_{t-i} + \sum_{i=1}^n b_2 \Delta \ln GDP_{t-i}^2 + \sum_{i=1}^n b_3 \Delta \ln EC_{t-i} + \sum_{i=1}^n b_4 \Delta \ln TOURI_{t-i} \quad (7)$$

$$+ \gamma_1 \ln CO_{2t-1} + \gamma_2 \ln GDP_{t-1} + \gamma_3 \ln GDP_{t-1}^2 + \gamma_4 \ln EC_{t-1} + \gamma_5 \ln TOURI_{t-1} + \mu_t$$

$$\Delta \ln GDP = \alpha_0 + \sum_{i=1}^n b_1 \Delta \ln EC_{t-i} + \sum_{i=1}^n b_2 \Delta \ln CO_{2t-i} + \sum_{i=1}^n b_3 \Delta \ln TOURI_{t-i} \\ + \lambda_1 \ln GDP_{t-1} + \lambda_2 \ln EC_{t-1} + \lambda_3 \ln CO_{2t-1} + \lambda_4 \ln TOURI_{t-1} + \zeta_t \quad (8)$$

To test the existence of a relationship of co -integration between variables, the procedure under - behind of Statistics is the F statistic of Wald test. The null hypothesis of the F- statistic is established as follows : for Eq. (7) and for Eq . (8). The F-statistic calculated in our study will be compared with the critical values from the table of Peseran et al. (2001). The decision on the existence of a cointegrating relation is confirmed if the calculated F-statistic is above the tabulated upper limit. However, if the F- statistic is between the bounds, no conclusion can be deduced and if the F- statistic is below the lower bound the null hypothesis of no cointegration is accepted. Table (2) shows the results of the hopping test.

Table 2: hop test

Variable dependent	lag selection	F- statistic	Decision
panelA (Morocco)			
F (CO2 \ GDP, GDP2, TR, EC)	(11, 0, 2, 0, 6)	5.498724	cointegrated
F (GDP \ EC, TR, CO2)	(6, 0, 2, 7)	6.871155	cointegrated
panel B (Egypt)			
F (CO2 \ GDP, GDP2, TR, EC)	(6, 6, 9, 1, 1)	6.252141	cointegrated
F (GDP \ EC, TR, CO2)	(3, 1, 4, 0)	6.394991	cointegrated
panel C (Tunisia)			

F (CO2 \ GDP, GDP2, TR, EC)	(3, 2, 2, 1, 3)	8.483235	cointegrated
F (GDP \ EC, TR, CO2)	(2, 2, 1, 2)	5.752371	cointegrated
		k = 4	k = 3
Lower-bound critical value at 5%		2.86	3.23
Upper-bound critical value at 5%		4.01	4.35
Lower-bound critical value at 1%		3.74	4.29
Upper-bound critical value at 1%		5.06	5.61

The results of table (3) show that the F- statistic for the two models are strictly greater than the upper limit of the threshold of 5% and 1% and that for the three countries, namely panel (A), panel (B) and panel (C) which brings us back to rejecting the null hypothesis of the absence of a cointegrating relationship between the variables studied. Therefore, we can conclude the existence of at least one cointegrating relationship between CO2 emissions and the other explanatory variables in the first relationship and also the existence of at least one cointegrating relationship between GDP and the other variables in the second relation and that for the three countries studied.

After verifying the existence of at least one cointegrating relation between the variables in the two relations, we study the long term and short term relation using the ARDL model. To determine the optimal delay length of equations (7) and (8) we used the Schwarz information criterion ; the maximum number we took is 12. The results of the delay choice are shown in Table (2). The coefficients of the long-term ARDL models of the three countries are presented in Table (3).

Table 3 : Long-term relationship

panel A (Morocco)				panel B (Egypt)					
variable	Dependent CO2 variable		Dependent variable gdp		variable	Dependent CO2 variable		Dependent variable gdp	
	Coefficient	T-Ratio	Coefficient	T-Ratio		Coefficient	T-Ratio	Coefficient	T-Ratio
GDP	7,299963	2.874072 **			GDP	5.9698	3.142 ***		
GDP2	-0.466836	-2.97542 ***			GDP2	-0.3262	-2.415 ***		
EC	1.797944	3.794058 ***	0.463774	2.954071 ***	EC	0.3551	3.639 ***	-0.0721	-0.80702
TR	0.214502	1.749531	0.133707	5.858203 ***	TR	-0.1589	-3.133 ***	0.2122	6.3910
CO2			0.197838	1.299729	CO2			0.2919	4.2726 ***
panel C (Tunisia)									
variable	Dependent CO2 variable		Dependent variable gdp						
	Coefficient	T-Ratio	Coefficient	T-Ratio					
GDP	-6.164247	-1.836526 **							
GDP2	0.388975	1.915138 **							
EC	0.744024	3.579334 ***	1.170426	2.193419 ***					
TR	0.054153	1.976515 **	0.091118	2.344256 ***					
CO2			0.322376	0.2299					

(***), (**) and (*) indicate statistical significance at 1%, 5% and 10% respectively

The results of the first relationship show that the coefficients associated with GDP are significant in the three countries of our analysis. Any increase in the level of long-term income by 1 point increases the quantities of CO₂ emitted, by 7.29 points in Morocco and 3.14 points in Egypt, while it reduces the quantities of CO₂ by 6.16 point in Tunisia. For the coefficients associated with energy consumption, we note that they are significantly positive in the three countries. Any increase in the levels of energy consumed increases the quantities of the pollutant and worsens the environmental situation. Our results are well compatible with various empirical works (Chebbi HE, 2010, 2011; Mehdi Ben Jebli Slim Ben Youssef 2015; Houda A and Belloumi M., 2016). The coefficient of the GDP² variable appears to be negatively significant in Morocco and Egypt and positively significant in Tunisia. This finding can inform us about the shape of the curvature between CO₂ emissions and income levels, in other words the verification of the Kuznets environmental curve. The negative sign of GDP² in Morocco and Egypt confirms that the relationship takes the form of an inverted U-curve while it is U-shaped in Tunisia. This result seems well in line with that of Mehdi B J, Slim SY 2015 in Tunisia. Finally, for the tourism variable, we notice that it admits a significantly negative coefficient in Egypt while this coefficient is significantly positive in Tunisia and positive and neutral in Morocco. A 1 percent increase in tourist arrivals in Egypt reduces the amount of CO₂ emitted by 0.15%. Indeed, tourism in Egypt is characterized by the dominance of cultural tourism through visits to archaeological areas. The positive effect of tourism on the quality of the environment in Egypt can also be explained by its effect on long-term growth. Indeed, the increase in the level of tourism increases the level of income which, for its part, reduces the quantities of the pollutant in the long term since the environment-growth relationship takes the form of a decreasing curve in the long term. According to the logic of the inverted U-shaped Kuznets environmental curve, the increase in income level reduces CO₂ emissions in the long run. However, the growth-environment relationship takes the form of a U in Tunisia. Long-term income growth causes CO₂ emissions to vary in the same direction. Thus, the increase in the number of tourists which increases the income per inhabitant stimulates the degradation of the environment in Tunisia. Also, tourism in Tunisia is characterized by seasonality. The more or less hot periods present the period of high season which requires additional amounts of energy for transport and air conditioning. Tourist arrivals play the role of a catalyst; its increase increases energy consumption, which in turn increases the quantities of CO₂ emitted into the atmosphere.

In the second relationship where the level of income is presented as a dependent variable, we notice that an increase in energy consumption of 1% increases the level of economic growth by 0.46% in Morocco and by 1.17% in Tunisia. This positive relationship is explained by the fact that these countries are in a growth phase; all economic development requires additional amounts of energy. For the tourism variable, we notice that it admits positively significant coefficients in the three countries. The 1% increase in tourist arrivals raises long-term income levels by 0.133% in Morocco, 0.212 in Egypt and 0.09 in Tunisia.

In a second step, the conditional ECM regression associated with the level relation in equations (5) and (6) is estimated. The ECM estimates are provided in Tables (4) and (5). The results presented in table (4) show that the ECT term associated with equations (5) is statistically significant and negative, which confirms the jump test on the existence of at least one relationship between the variables of the models in the long term. The ECT values illustrated in table (4) are of the order of ECT = -0.058 for Morocco, ECT = -0.2 for Egypt and ECT = -0.279 for Tunisia, which implies that the emissions of CO₂ converge towards long-term equilibrium at a rate of 5.8% in Morocco 20%, in Egypt and 27.9% in Tunisia through the

channels of economic growth, energy consumption and tourism. Tunisia's speed of adjustment to the equilibrium is higher than that of Egypt and Morocco. For the short-term coefficients of energy consumption we notice that they are positive and statistically significant at date (t) while they are negative and statistically significant for previous periods. However, the associated short-term coefficients of economic growth (GDP) are negative and statistically significant in period (t), but become positive in later periods. Finally, we note that the tourist variable admits a negative and non-significant coefficient in Morocco and a positive and statistically significant coefficient in Egypt and Tunisia.

Table 4 : Short-term relationship of the relationship (CO2 / GDP , GDP2, EC, TOURI)

Panel A (Morocco)				Panel B (Egypt)				Panel C (Tunisia)			
Lag structure: (6, 6, 9, 1, 1)				Lag structure: (11, 0, 2, 0, 6)				Lag structure: (3, 2, 2, 1, 3)			
Variable	Coefficient	t-Statistic	Prob.	Variable	Coefficient	t-Statistic	Prob.	Variable	Coefficient	t-Statistic	Prob.
D (LNCO2 (-1))	0.613307	8.297709	0.000	D (LNCO2 (-1))	0.74823	9.4071	0.000	D (LNCO2 (-1))	0.499588	6.403396	0.000
D (LNCO2 (-2))	0.140828	2.183876	0.031	D (LNCO2 (-2))	0.35882	3.5266	0.000	D (LNCO2 (-2))	0.265285	3.156170	0.002
D (LNCO2 (-3))	0.080637	1.232608	0.220	D (LNCO2 (-3))	0.1874	2.2752	0.025	D (LNGDP)	-14.38558	2.720700	0.007
D (LNCO2 (-4))	-0.676143	9.042851	0.000	D (LNCO2 (-4))	-0.9259	-11.160	0.000	D (LNGDP (-1))	10.64071	2.036875	0.043
D (LNCO2 (-5))	0.455094	5.653720	0.000	D (LNCO2 (-5))	0.72386	6.1430	0.000	D (LNGDP2)	0.912852	2.676042	0.008
D (LNEC)	1.216525	14.57762	0.000	D (LNCO2 (-6))	0.34540	2.6769	0.008	D (LNGDP2 (-1))	-0.674859	1.997371	0.048
D (LNEC (-1))	-0.571452	3.404386	0.001	D (LNCO2 (-7))	0.08469	1.1489	0.253	D (LNEC)	-0.105820	0.993243	0.322
D (LNEC (-2))	-0.073619	0.497660	0.619	D (LNCO2 (-8))	-0.4948	-6.6577	0.000	D (LNTOUR)	0.135617	4.674990	0.000
D (LNEC (-3))	-0.499754	2.921283	0.004	D (LNCO2 (-9))	0.36598	4.2834	0.000	D (LNTOUR I(-1))	-0.021625	0.471517	0.638
D (LNEC (-4))	0.714049	3.406478	0.000	D (LNCO2 (-10))	0.17613	2.1286	0.035	D (LNTOUR I(-2))	-0.053228	2.155370	0.033
D (LNEC (-5))	-0.320145	2.778916	0.006	D (LNEC)	0.07194	3.2584	0.001				
D (LNGDP)	-5.701172	3.206264	0.001	D (LNGDP)	-0.0986	-0.1808	0.856				
D (LNGDP (-1))	0.121264	1.243510	0.216	D (LNGDP (-1))	0.9225	2.5121	0.013				
D (LNGDP (-2))	0.039495	0.408599	0.683	D (LNGDP2)	-0.0660	-2.4739	0.015				
D (LNGDP (-3))	0.126298	1.057270	0.292	D (LNTOUR)	0.07966	2.6743	0.008				
D (LNGDP (-4))	-0.215218	1.861903	0.065	D (LNTOUR I(-1))	-0.0684	-1.7670	0.080				
D (LNGDP (-5))	0.102971	1.128143	0.262	D (LNTOUR I(-2))	0.00830	0.2831	0.777				
D (LNGDP (-6))	0.031723	0.350230	0.726	D (LNTOUR I(-3))	-0.1421	-3.8997	0.000				

D (LNGDP (-7))	-	0.393		D (LNGDP (-7))	-0.079846	0.857440	3	D (LNTOUR I(-4))	0.25253	5.2752	0	0.000		
D (LNGDP (-8))	0.104426	1.890129	6	D (LNGDP (-8))	0.104426	1.890129	6	D (LNTOUR I(-5))	-0.0946	-3.2203	7	0.001		
D (LNGDP2)	0.374780	3.072586	7	D (LNGDP2)	0.374780	3.072586	7							
D (LNTOUR I)	-	0.204	0	D (LNTOUR I)	-0.023739	1.278643	0							
ECT	-0.058984	2.909441	5	ECT	-0.058984	2.909441	5	ECT	-0.2025	-4.7835	0	0.000		
								ECT	-0.279655	6.080513	0	-	0.000	

The results presented in table (5) of the estimate of the ECM of equation (6) clearly illustrate negative and statistically significant ECTs at the 5% level, which confirms the existence of at least one relation of long term between the model variables. Economic growth is converging towards its long-term equilibrium with an adjustment speed of around 25.7% in Morocco, 5.8% in Egypt and 2.1% in Tunisia. The coefficients associated with tourism are positive and statistically significant at the 5% threshold at date (t). For the energy consumption variable, its coefficient is positive and statistically significant in Morocco and Tunisia, while it is not significant in Egypt. The economic growth of the countries studied reacts to its long-term trajectory significantly in the model induced through tourism.

Table 5 : Short-term relationship of the relationship (GDP / CO2 , EC, TOURI)

Panel A				Panel B				Panel C			
Lag structure: (3, 1, 4, 0)				Lag structure: (6, 0, 2, 7)				Lag structure: (2, 2, 1, 2)			
Variable	Coefficient	t-Statistic	Prob.	Variable	Coefficient	t-Statistic	Prob.	Variable	Coefficient	t-Statistic	Prob.
D (LNGDP (-1))	0.431394	5.227675	0	D (LNGDP (-1))	0.542618	6.261703	0	D (LNGDP (-1))	0.489665	6.432117	0
D (LNGDP (-2))	0.204351	2.253400	0	D (LNGDP (-2))	0.200589	2.178307	5	D (LNEC)	0.278847	6.818410	0
D (LNCO2)	-0.248970	-1.69609	4	D (LNGDP (-3))	0.051345	0.584011	4	D (LNEC (-1))	-0.131959	2.984630	4
D (LNEC)	0.856470	4.311944	0	D (LNGDP (-4))	-0.375490	3.875753	2	D (LNCO2)	-0.048952	1.662522	9
D (LNEC (-1))	-0.084230	-0.29947	1	D (LNGDP (-5))	0.242708	2.905559	4	D (LNTOUR I)	0.028212	2.360695	8
D (LNEC (-2))	0.014055	0.051903	7	D (LNEC)	-0.004242	0.825483	9	D (LNTOUR I(-1))	-0.020825	1.900751	7
D (LNEC (-3))	-0.233166	-1.54848	1	D	-	-	0.428				
D (LNTOUR I)	0.034386	3.760381	3	(LNCO2)	-0.011710	0.794851	4				
				D (LNCO2 (- 1))	0.005022	0.334780	4				
				D (LNTOUR I)	0.038510	5.658170	0				
				D (LNTOUR I(-1))	-0.006135	0.452129	1				
				D (LNTOUR I(-2))	-0.013227	1.259856	4				
				D (LNTOUR I(-3))	-0.035597	3.601703	5				

				D					
				(LNTOUR				0.000	
				I(-4))	0.051533	4.102948	1		
				D					
				(LNTOUR				0.459	
				I(-5))	-0.009330	0.742585	3		
				D					
				(LNTOUR				0.073	
				I(-6))	-0.012447	1.806518	5		
								0.000	
ECT	-0.257175	-	0.000						0.033
		5.095588	0	ECT	-0.058796	5.018204	0	ECT	-0.021006
									2.147189
									7

5. Conclusion

The objective of this study is to examine the role of tourism development on growth and environmental quality in three countries of North Africa (Morocco, Egypt and Tunisia). The study used two major equations, the first is used for the assessment of the environmental Kuznets curve (CEK) by integrating economic growth (square of GDP per capita), carbon emissions, tourism arrivals and energy consumption while the second equation is used to study the impact of energy consumption, environmental quality and tourism arrivals on economic growth. The introduction of energy consumption into the equations is used to clarify the transmission channels of the effects of tourism on the quality of the environment. The results show that tourism has a direct and statistically significant impact on the level of carbon dioxide emissions and economic growth in the long term period of the economies studied. The results also confirm the existence of an inverted U-shaped relationship for Morocco and Egypt between CO₂ emissions and income level, while this relationship takes the form of a U in Tunisia. The error correction models in the present study have shown that (1) CO₂ emissions converge towards their long-term equilibrium situation with a speed of the order of 5.8% in Morocco 20% in Egypt and 27.9% in Tunisia through the channels of economic growth of energy consumption and tourism. This finding reveals that the growth of tourism significantly allows climate change to rise to high levels. (2) economic growth converges towards its long-term equilibrium by an adjustment speed of the order of 25.7% in Morocco, 5.8% in Egypt and 2.1% in Tunisia.

The results of the present study suggest some implications. The degradation of the quality of the environment is reinforced initially with the increase in the level of income, after having reached a certain level of threshold, the quality of the environment improves gradually in a second time with the levels of income.

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Effect of Salicylidene Salicylhydrazide on Testes of Albino Mice: A Histomorphological Study

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Abstract: There is recently an increasing reports of reduction in sperm counts along with other reproductive disorders that is ascribe to the use of drugs and environmental chemicals. In this regard conducting toxicological studies on male reproductive is of paramount importance. This study evaluates salicylidene salicylhydrazide (SCS) for any possible toxicological effects on male reproductive system. Male BALB/c mice were daily administered withSCSat 5, 25, and 50 mg/kg for 7 and 14 days. The body and testes weights were measuredand the testes were subjected to histological tissue processing techniques. The extent of testicular toxicity was evaluated by using modified Johnsen scoring system for assessing the level of spermatogenesis, and morphometric analysis by measuring the diameter of the seminiferous tubules, thickness of germinal epithelium, and area of interstitial cells of Leydig. The body and testes weights showed that the various doses of SCS have no substantial effects after 7 and 14 days. The tested doses of SCS did not produce any distinguishable change in the normal histological features of seminiferous tubules and interstitium after 7 days. However, after 14 days, the 50 mg/kg dose of SCS was associated with vacuolization and loosening of germinal epithelium. These mild-to-moderate histopathological aberrations was confirmed from morphometric analysis in this dose group in which a decrease in the seminiferous tubules diameter and reduction in the thickness of germinal epithelium along with an increase in the interstitial area were observed. These findings concluded that SCS is considered to be relatively safe.

Key words: Testicular toxicity evaluation, reproductive toxicity assessment, germinal epithelium, spermatogenesis.

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1.Introduction

The preclinical testicular toxicity evaluation of potential drug-like compounds is important and is a standard component of safety assessment during drug development process (Hukkanen et al., 2016). Drugs as well as environmental pollutants have shown to greatly affect the spermatogenesis process during different stages of development in humans. These include cadmium, which severely affect the normal testicular function parameters including decrease testes weight, reproductive hormones, production of oxidative stress and induction of apoptosis in testes (Nna et al., 2017). Conducting toxicological studies on male reproductive system have received greater attention in recent years due to the increasing reports of reduction in the sperm counts along with other reproductive disorders including testicular cancer and possible transmission of exposure-related to the fetus (Cyr, 2016).

Various scientific techniques can be used to evaluate the male reproductive toxicology and these includes general systemic toxicity testing, assessing the functional effects on the reproductive organs of male, as well as mechanistic and molecular approaches conducted at the tissue level or in isolated cells (Coder et al., 2010). However, assessing the toxicological effect on the male reproductive system in humans is challenging as only a few clinical toxicological markers are available that can monitor possible alterations in testicular function including analysis of semen, testosterone and gonadotropin concentrations in the serum. Moreover, the real time monitoring of adverse effects on testicular function in humans is also difficult due to the several months of latency period between the time of injury to the seminiferous tubules and the time of its clinical presentation and detection by semen analysis. There is also a dilemma of correlating the measurements of testicular function to changes and effects on male fertility (Hukkanen et al., 2016).

Salicylidene salicylhydrazide is the derivative of salicylaldehyde benzoylhydrazone and synthesized by converting alkyl ester to hydrazide by refluxing with excess hydrazine hydrate and addition of aromatic aldehyde (Ainscough et al., 1999). It has a molecular weight of 256.26 g/mol and a melting point of 284-287 °C. It is observed that salicylidene salicylhydrazide has a strong cancer cell damaging potential as it strongly inhibited the growth of human colon adenocarcinoma cells. Its inhibitory anticancer potential (IC_{50}) is reported as 1.8, which is more potent than cisplatin (4.2) against these cancer cell lines (Ainscough et al., 1999). It also strongly inhibits synthesis of DNA in the rodent leukemia and hepatoma cancer cells, human bladder cancer, lung carcinoma and melanoma cells (Johnson et al., 1982). Moreover, it also has $\beta 1$ subunit containing GABA_A receptors inhibitory affinity and the interaction may involve an allosteric mechanism (Thompson et al., 2004). Salicylidene salicylhydrazide has an analgesic potential that can be useful for treating peripheral neuropathic pain conditions linked with chemotherapy (Rukh et al., 2020). The present study evaluated salicylidene salicylhydrazide (SCS) for any possibility of producing toxicological effects on the male reproductive system, which may compromise its otherwise beneficial effectiveness in disease-state conditions.

2. Materials and Methods

2.1 Chemicals

Salicylidene salicylhydrazide (97%) was obtained from Alfa Aesar, Thermo Fisher Scientific, Kandel, Germany. It was dissolved in a vehicle consisting of DMSO, Tween80 and normal saline in a ratio of 3:1:96.

2.2 Animals

Male BALB/c mice weighing 20-40 g were included in the study. They were acclimatized in a light dark cycle of 12/12 h at 20-24°C. The experiments were approved by the Ethical Committee of Khyber Medical College, Peshawar, Pakistan and approval for the study was granted vide registration number 42/PG/KMC.

2.3 Experimental design

The mice were divided into four main groups (A, B, C and D), while groups B, C and D were the experimental groups. Each group was further subdivided into two subgroups i.e. A1, A2, B1, B2, C1, C2, D1 and D2. Each subgroup comprised of 6 animals. Animals of each subgroup were kept in a separate cage. The subgroup A1 was the control group for B1, C1 and D1 experimental subgroups, while the subgroup A2 was the control group for experimental subgroups of B2, C2 and D2. Animals in the control subgroups A1 and A2 received the vehicle (3% DMSO, 1% Tween80 and 96% normal saline) for 7 and 14 days, respectively. The animals in subgroups B1, C1 and D1 received SCS once daily through the intraperitoneal route at doses of 5 mg/kg, 25 mg/kg and 50 mg/kg, respectively for consecutive 7 days. Likewise, SCS was intraperitoneally administered to animals in subgroups B2 at 5 mg/kg, C2 at 25 mg/kg and D2 at 50 mg/kg for consecutive 14 days. The experimental plan is shown in Table 1.

Table 1: Experimental plan

Groups	Subgroups	Dose of drug
Control Group A	A1 (<i>n</i> = 6)	10 ml/kg (3% DMSO, 1% Tween80 and 96% normal saline) for 7 days
	A2 (<i>n</i> = 6)	10 ml/kg (3% DMSO, 1% Tween80 and 96% normal saline) for 14 days
Experimental Group B	B1 (<i>n</i> = 6)	5 mg/kg for 7 days
	B2 (<i>n</i> = 6)	5 mg/kg for 14 days
Experimental Group C	C1 (<i>n</i> = 6)	25 mg/kg for 7 days
	C2 (<i>n</i> = 6)	25 mg/kg for 14 days
Experimental Group D	D1 (<i>n</i> = 6)	50 mg/kg for 7 days

D2 ($n = 6$)

50 mg/kg for 14 days

2.4 Histological study

At the end of 7 and 14 days, the animals were sacrificed and their testes were surgically removed. The testes were weighed along with epididymis. They were then placed in labeled jars containing 10% neutral buffered formaldehyde. After 48 hours, the tissues were dehydrated in graded ethanol solutions (70-100%), each for 1 h. The tissues were then cleared in alcohol-xylene solution and then in 100% xylene with two changes each for 1 h at 45-47°C under constant stirring. The tissues were then infiltrated with paraffin wax and were then embedded. The embedded tissues were sectioned through a rotary microtome at 4-5 micron and were then stained with hematoxylin and eosin and periodic acid-Schiff for microscopic evaluation (Creasy, 2002; Shahid & Subhan, 2014; Shahid & Subhan, 2014).

2.5 Microscopic examination for histological changes

The tissue slides were examined under a light microscope for various parameters including degeneration of germ cells, multinucleate aggregation, depletion of germ cells, exfoliation of germ cells, vacuolization of the germinal epithelium of the seminiferous tubules, contraction of tubules, dilatation of tubules, retention of spermatids, necrosis of the seminiferous tubules, atrophy, hypertrophy, hyperplasia and adenoma of Leydig's cell and disorganization of the tubular contents. The histopathological changes occurring in the testis were examined under a 400x original magnification using a trinocular microscope. The level of spermatogenesis was evaluated using the modified Johnsen scoring system (Mustafa, 2019).

2.6 Morphometry

The morphometric analysis was performed for the measurement of seminiferous tubular diameter, germinal epithelium thickness, and area of interstitial cells of Leydig under high power field. These measurements were conducted using the Nikon microscope (ECLIPSE Ci-L) with a standalone camera control unit (DS-L3).

2.7 Statistical analysis

The histopathological changes were evaluated by an experienced pathologist who was blinded to the various treatment groups. The quantitative data were expressed as mean \pm standard deviation (SD) or standard error of the mean (SEM). Statistical analyses were carried out using one-way ANOVA or two-way repeated measures ANOVA followed by appropriate *post hoc* tests. A *P* value less than 0.05 was accepted as statistically significant.

3. Results

3.1 Effect of salicylidene salicylhydrazide on gross physical change

After 7 days, the group of mice treated with the vehicle (A1) showed a normal gross behavioral profile. Each mouse was observed to perform both individual and social behaviors. Most of the time the animals were active and were actively performing their exploratory behavior. The mice in the subgroups administered with the tested doses of SCS at 5, 25 and 50 mg/kg (groups B1, C1

and D1) were also observed to perform their normal general activity. The animals were found to be busy in their affiliative interactions in their respective cages. The breathing patterns were also observed to be normal and the animals exhibited typical locomotor behavior with a normal gait. Moreover, no aggressive behaviors were observed during the 7 days of observation,

After 14 days, the group of mice treated with the vehicle (A2) exhibited a normal behavioral and locomotor profile. The animals that were administered with the 5, 25 and 50 mg/kg doses of SCS (groups B2, C2 and D2) were also grossly observed after dosing in their respective cages. It was found that these doses have no gross effect on the behavior as well as on the locomotion. The animals in all the experimental groups exhibited a normal exploratory sequence of searching, attending, approaching and investigating behaviors. Moreover, the different subgroups of animals did not show any signs and symptoms that may suggestive of any underlying painful conditions.

3.2 Effect of salicylidene salicylhydrazide on body weight

After 7 days of consecutive treatment with SCS, the animals in the various groups did not show any statistically significant change in the body weight as no significant difference was observed in the groups of mice administered with SCS at the tested doses of 5, 25 and 50 mg/kg (groups B1, C1 and D1) as compared to the vehicle treated group (group A1). Similarly, administration of SCS for 14 days has no significant effect on the body weight of animals allocated to the various treated groups (groups B2, C2 and D2) when compared to the corresponding vehicle treated group (group A2), on the 14th day of the experimental duration (Figures 1A and 1B).

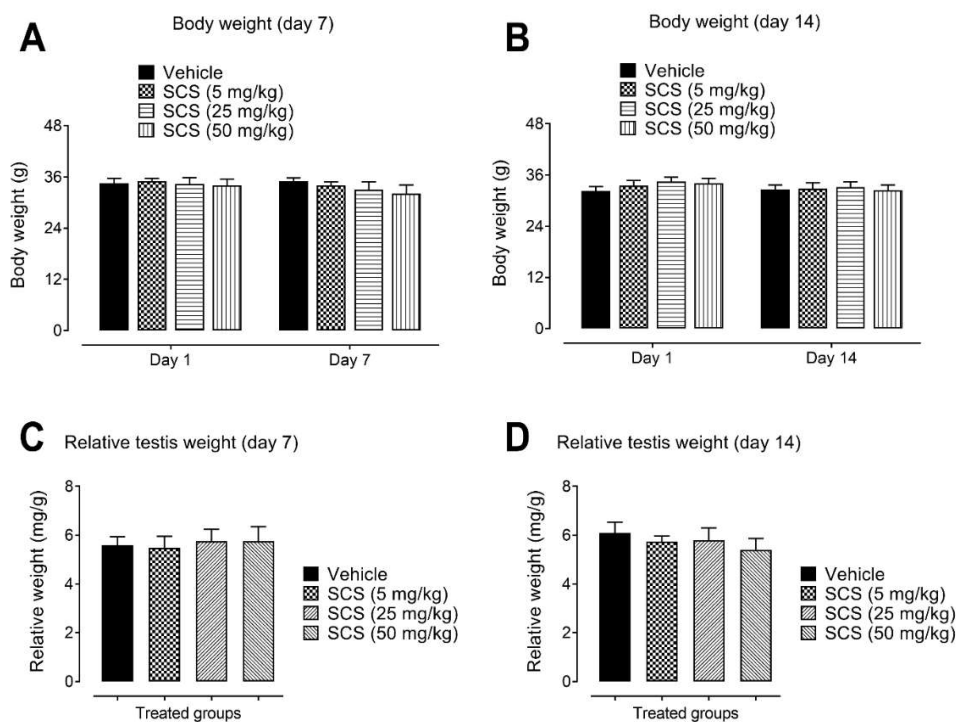


Figure 1: Effect of salicylidene salicylhydrazide (SCS) at 5, 25, and 50 mg/kg on body weight (A and B) and relative testes weight (C and D) after 7 and 14 days of administration. Each column represents mean body weight or relative testes weight in grams (g) or milligrams (mg) \pm SEM. SCS groups were compared with the vehicle groups. No significant difference was observed, two-way repeated measures ANOVA followed by Dunnett's *post hoc* test, $n = 6$ mice per group.

3.3 Effect of salicylidene salicylhydrazide on relative testes weight

The ratio of the weight of the testes to the body weight of the respective animal was calculated to ascertain any gross toxicological changes irrespective of any influential differences occurring in the body weight. The relative weights of the testes were not found to show any drastic variation among the various treated groups after experimental time-period of 7 days. The groups of mice administered with SCS at 5, 25 and 50 mg/kg (groups B1, C1 and D1) did not show any significant difference in the ratio of the testes weights to their corresponding body weights expressed as milligram of testis weight to body weight in grams, when compared to the control group of mice administered with the vehicle (group A1). Likewise, the relative testis weight of the treated groups was not grossly deviated from each other after 14 days of treatment with SCS (groups B2, C2 and D2) as compared to corresponding relative testes weights of the control group mice treated with the vehicle (group A2) (Figures 1C and 1D).

3.4 Effect of salicylidene salicylhydrazide on gross appearance of the testes

The control groups (A1 and A2) displayed a normal appearance of both testes and the attached epididymis with a higher reflectivity. They appear ovoid and possess a medium level reflectivity. Similar characteristics of testes have been observed in the experimental subgroups. Examination of the testes from the subgroups of mice treated with SCS at 5 mg/kg (B1 and B2), 25 mg/kg (C1 and C2) and 50 mg/kg (D1 and D2) showed that there was no change in the shape, color and texture of the testes and any gross abnormalities.

3.5 Effect of salicylidene salicylhydrazide on testes histology

The vehicle administered animals (groups A1 and A2) showed a normal histological feature of the testicular tissue. The seminiferous tubules were lined by germinal epithelium in which various germ cells were distributed. The cells of spermatogonia were found adjacent to the basement membrane, while the primary spermatocytes were distributed in the basal as well as in the middle compartments of the germinal epithelium. A large number of rounded spermatids were visible in the middle as well as in the adluminal compartments of the seminiferous tubules. Moreover, the elongated spermatids were found in the adluminal compartment of the seminiferous tubules. Their heads were visible to be embedded in the supporting Sertoli cells while their tail was protruding into the lumen of the seminiferous tubule. The seminiferous tubules were separated by a connective tissue septum. The interstitial spaces among the tubules contained the interstitial cells of Leydig. There were also blood vessels containing red blood cells in their lumen visible in the interstitial spaces among the seminiferous tubules.

The administration of SCS to mice for 7 days showed a normal histology of the seminiferous tubules. The different features of the germinal epithelium including the arrangement of the spermatogonia at the basal region, the primary spermatocytes at adluminal region, presence of

Sertoli supporting cells, the distribution of spermatids and the interstitial region were appeared normally in the different groups of animals administered with SCS at doses of 5 mg/kg (group B1), 25 mg/kg (group C1) and 50 mg/kg (group D1) (Figures 2 and 3). The animals administered with SCS for 14 days at doses of 5 mg/kg (group B2) and 25 mg/kg (group C2) showed a normal histological feature of the seminiferous tubules in which the spermatogonia was found in the basal compartment of the tubules along with some primary spermatocytes. The primary spermatocytes were also found in the middle compartment of the seminiferous tubules. Numerous rounded and elongated spermatids were visible in the adluminal and luminal regions of the germinal epithelium. The supporting Sertoli cells as well as interstitial cells of Leydig were observed to be normally distributed in the germinal epithelium of the seminiferous tubules. The group of animals treated with SCS at a higher dose of 50 mg/kg (group D2) was also presented with a normal distribution of germ cells in the different regions of the seminiferous tubules. However, in some animals the germinal epithelium contained small vacuoles that are unevenly distributed, while in other seminiferous tubules, a loosening of the germinal epithelium was observed (Figures 4 and 5).

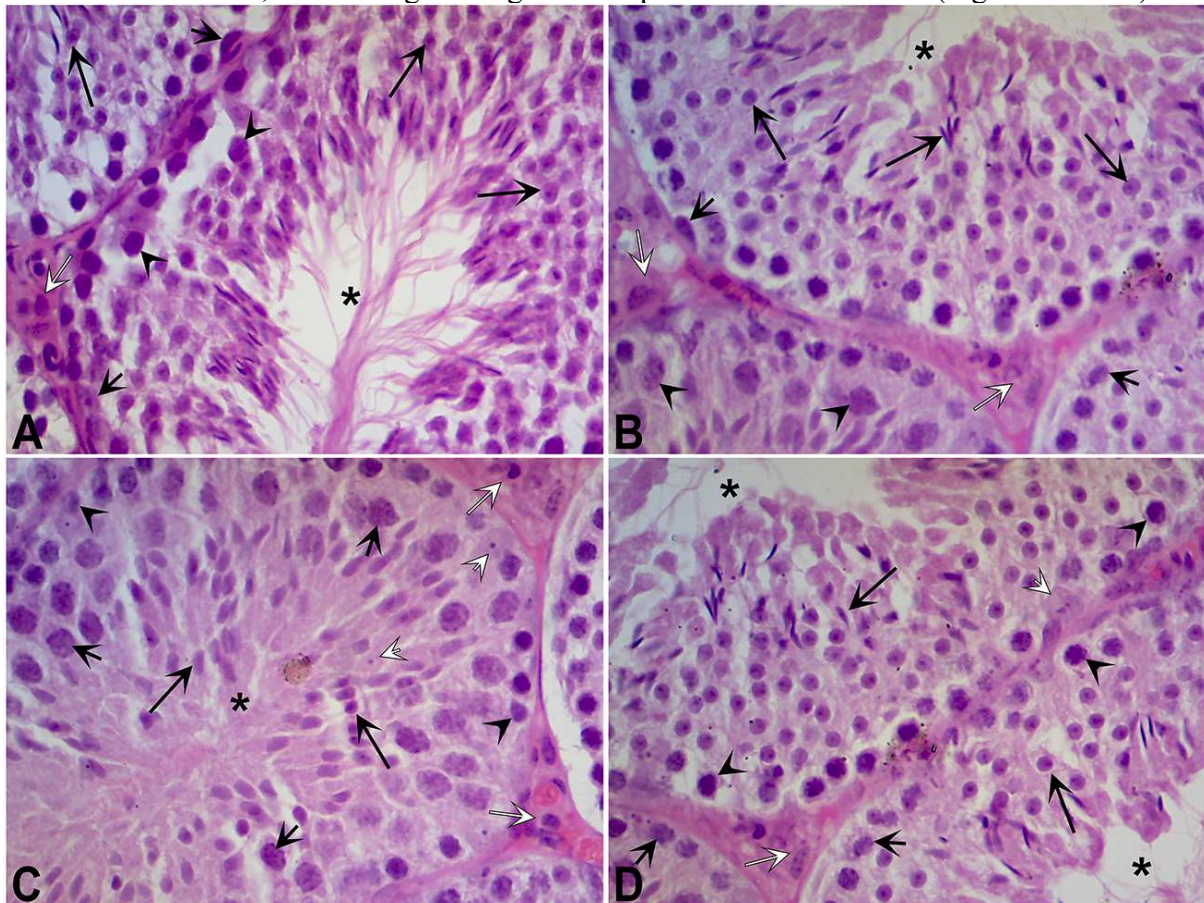


Figure 2: Representative photomicrographs (H&E, 400x) of the germinal epithelium of seminiferous tubules from testes of mice after 7 days of treatment with vehicle (A) showing normal histology of dark and pale spermatogonia (arrow heads), numerous pachytene spermatocytes (small arrows), rounded and elongated spermatids (large arrows) with their tails protruding into the lumen (asterisk), and Leydig cells (white arrow) in the interstitial

compartment. Normal histological features of the germinal epithelium were observed in the testes of mice treated with SCS at 5 mg/kg (B), 25 mg/kg (C), and at 50 mg/kg (D).

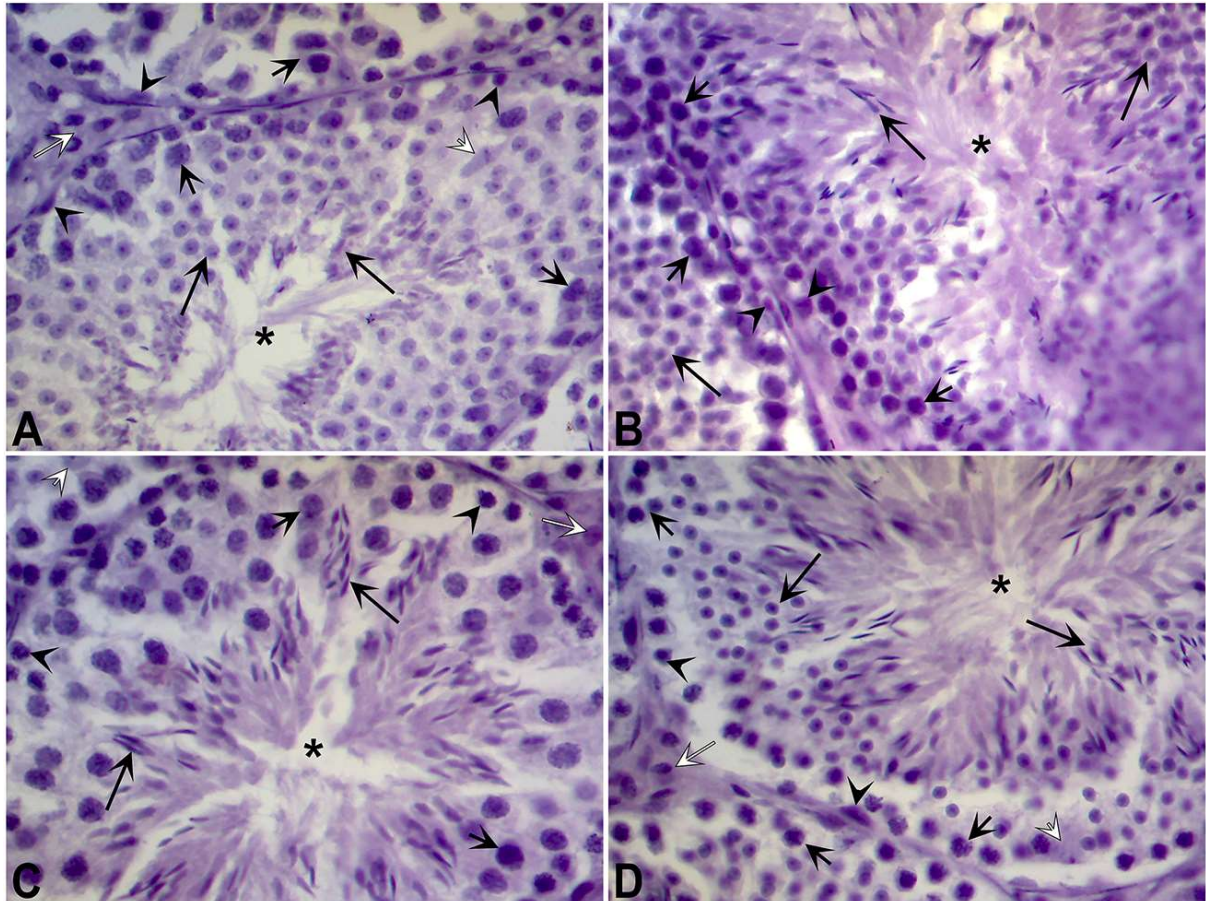


Figure 3: Representative photomicrographs(PAS, 400x) of a section of germinal epithelium from the testes of mice after 7 days of administration with the vehicle (A) showing the normal histology of interstitial cells of Leydig (large white arrow), pale and dark spermatogonia (arrow heads), primary spermatocytes (small arrows), numerous rounded spermatids (large arrow) with tails of elongated spermatids (large arrow) appeared protruding into the lumen and Sertoli cell (small white arrow). Normal histology of germinal epithelium lining the seminiferous tubules was observed in the group of mice treated with SCS at 5 mg/kg (B), 25 mg/kg (C), and 50 mg/kg (D).

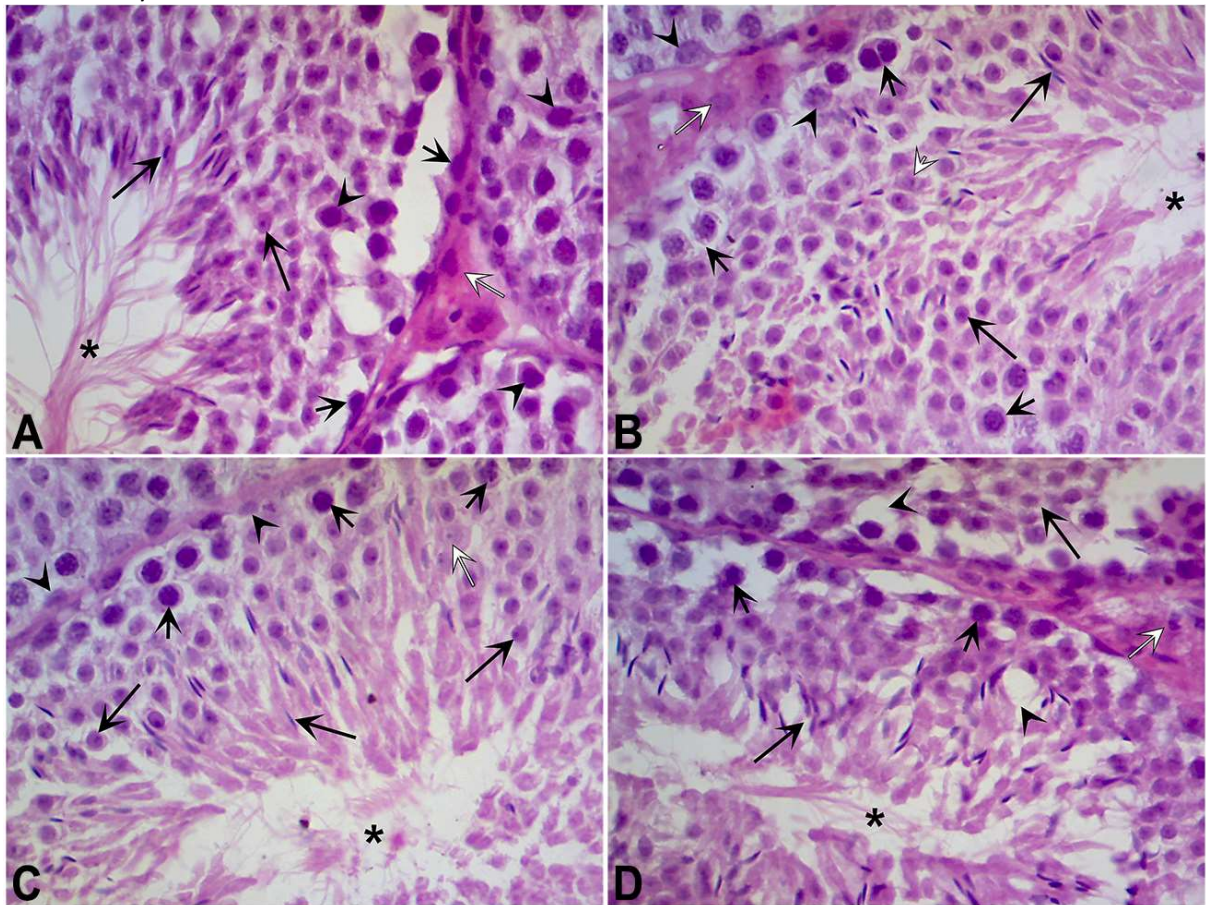


Figure 4: Representative photomicrographs (H&E, 400x) of the germinal epithelium of seminiferous tubules from testes of mice after 14 days of treatment with vehicle (A) showing normal histological appearance of spermatogonia (small arrows), pachytene spermatocytes (arrow heads), rounded spermatids (large arrow) as well as elongated spermatids (large arrow) with their tails extending into the luminal space (asterisk) and numerous interstitial cells of Leydig (white arrow). Normal histology of the germinal epithelium cells lining the seminiferous tubules was observed in the testes of mice treated with SCS at 5 mg/kg (B), 25 mg/kg (C), and 50 mg/kg (D). The major histopathological finding in the 50 mg/kg treated group (D) was the epithelial vacuolization as revealed from the numerous vacuoles (arrow heads) that are visible in the germinal epithelium.

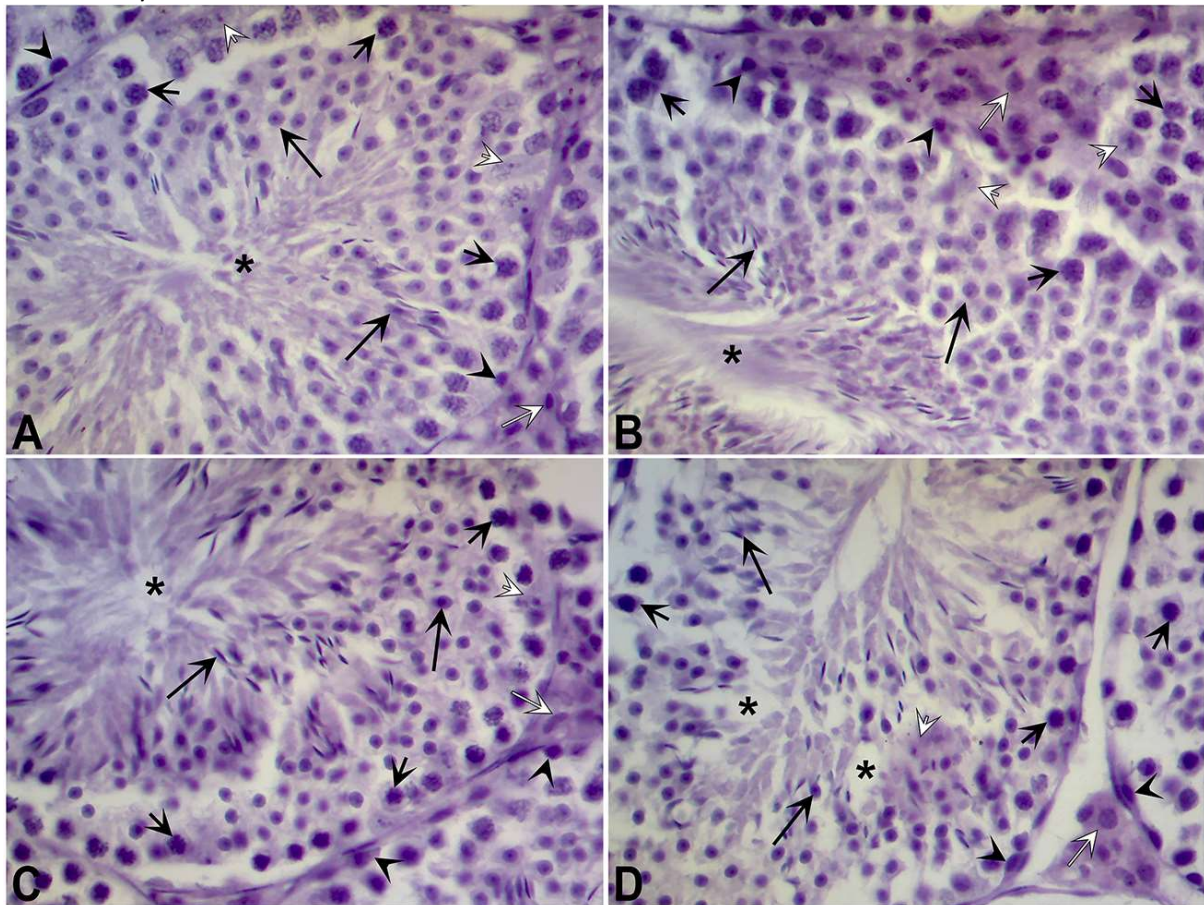


Figure 5: Representative photomicrograph (PAS, 400x) of a section of germinal epithelium from the testes of mice after 14 days of administration with the vehicle (A) showing normal histological appearance of spermatogonia (arrow heads), primary spermatocytes (small arrows), Sertoli cells (small white arrow), numerous rounded spermatids (large arrow) with their tails extending into the lumen (asterisk), and interstitial cells of Ledig (large white arrow). Normal appearing germ cells are visible in the groups of animals treated with SCS at 5 mg/kg (B), 25 mg/kg (C), and 50 mg/kg (D). In the 50 mg/kg SCS group (D), there is loosening of the germinal epithelium containing vacuoles (asterisks) and dilatation of interstitial space.

3.6 Effect of salicylidene salicylhydrazide on seminiferous tubules diameter

The different groups of animals administered with the tested doses of SCS at 5, 25 and 25 mg/kg (groups B1, C1 and D1) have shown no significant alterations, when their diameters were measured as compared to the vehicle treated control animals group (group A1) after 7 days. After 14 days, the groups of animals administered with SCS at 5, 25 and 50 mg/kg (groups B2, C2 and D2) showed a non-significant decrease in their seminiferous tubules diameter when compared to that of the vehicle treated animals group (Figures 6A and 6B).

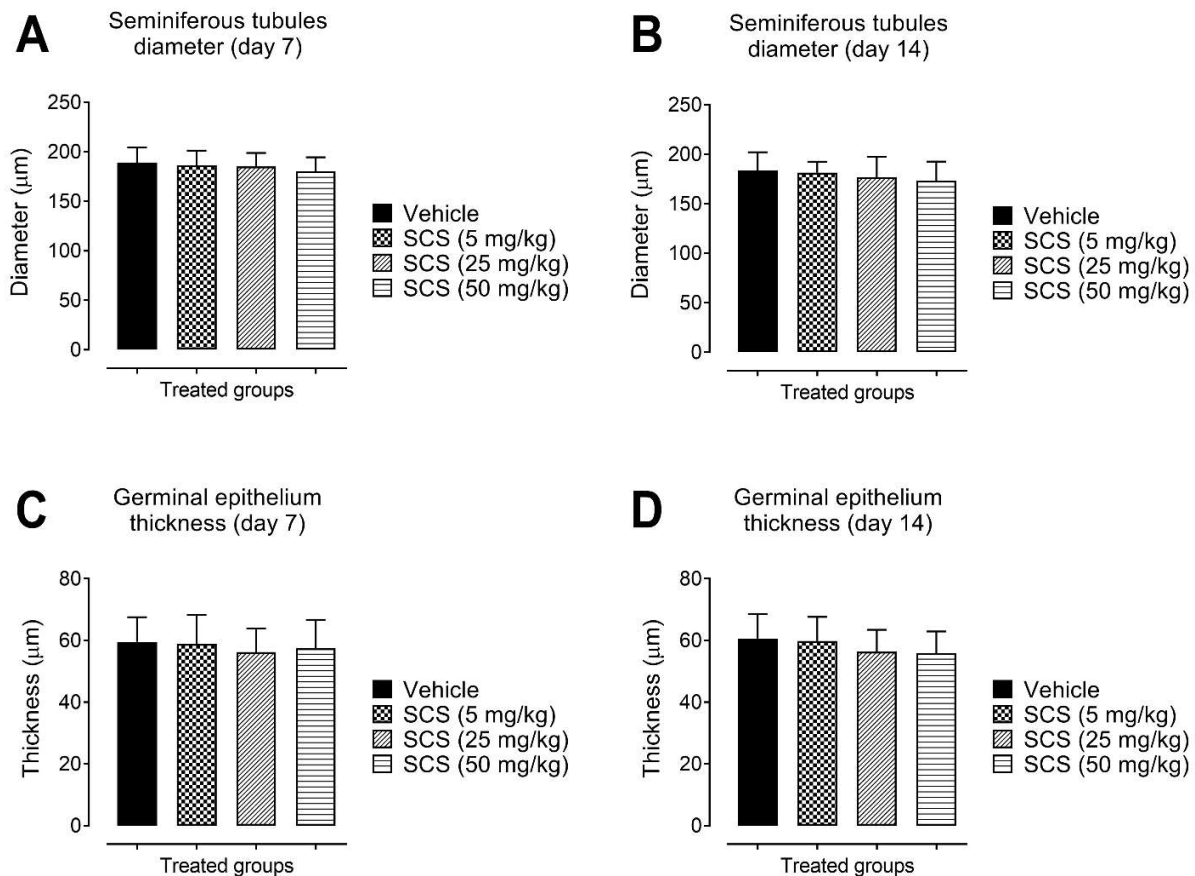


Figure 6: Effect of salicylidene salicylhydrazide (SCS) at 5, 25, and 50 mg/kg on seminiferous tubules diameter (**A and B**) and germinal epithelium thickness (**C and D**) after 7 and 14 days of administration. Each column represents mean seminiferous tubules diameter or germinal epithelium thickness in $\mu\text{m} \pm \text{SD}$. SCS groups were compared with the vehicle groups. No significant difference was observed, one-way ANOVA followed by Dunnett's *post hoc* test, $n = 25$ tubules per group.

3.7 Effect of salicylidene salicylhydrazide on germinal epithelium thickness

The groups of animals administered with the tested doses of SCS at 5, 25 and 50 mg/kg (groups B1, C1 and D1) showed no significant changes in the height of the germinal epithelium lining the seminiferous tubules, when compared to the epithelial thickness of the vehicle treated control animals group after 7 days. The groups of animals administered with SCS at 5, 25 and 50 mg/kg (groups B2, C2 and D2) showed a non-significant dose-dependent reduction in the height of germinal epithelium, with a prominent decrease was noted with the higher dose treated group i.e. 50 mg/kg as compared to the vehicle administered control group (group A2) after 14 days of experimental duration (Figure 6C and 6D).

3.8 Effect of salicylidene salicylhydrazide on Leydig cells area

After 7 days, the groups of animals administered with SCS at 5, 25 and 50 mg/kg (groups B1, C1 and D1) showed no apparent change in the area among the seminiferous tubules in addition to a slight increase for the 50 mg/kg treated animals group, as compared to the vehicle treated animals control group (group A1). After 14 days, the groups of animals treated with SCS at 5, 25 and 50 mg/kg (groups B2, C2 and D2) produced a non-significant dose-dependent increase in the area of the interstitial space among the seminiferous tubules when compared to the vehicle treated group (group A2) (Figures 7A and 7B).

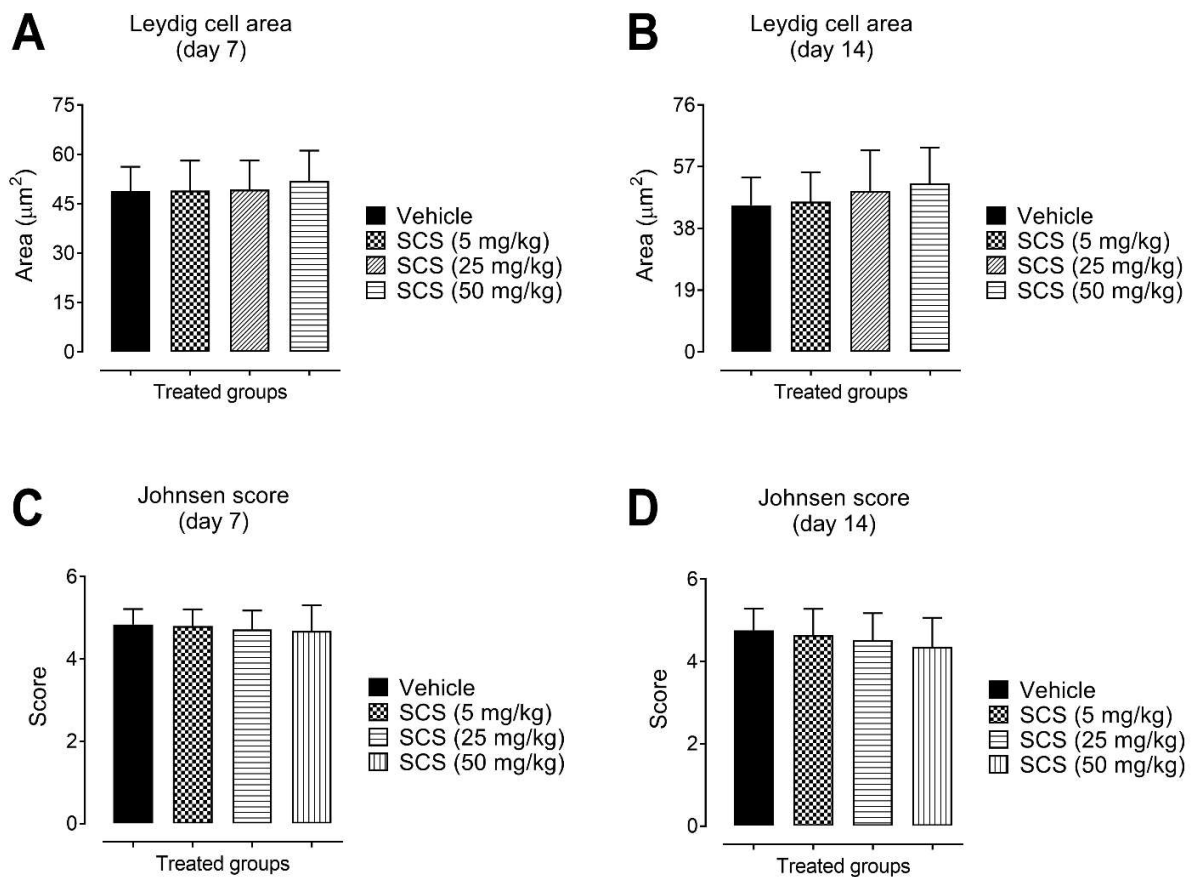


Figure 7: Effect of salicylidene salicylhydrazide (SCS) at 5, 25, and 50 mg/kg on Leydig cell area (A and B) and spermatogenesis using modified Johnsen score (C and D) after 7 and 14 days of administration. Each column represents mean Leydig cell area in μm^2 or Johnsen scores \pm SD. SCS groups were compared with the vehicle groups. No significant difference was observed, one-way ANOVA followed by Dunnett's *post hoc* test, $n = 25$ areas per group.

3.9 Effect of salicylidene salicylhydrazide on spermatogenesis

The groups of mice treated with SCS at 5, 25 and 50 mg/kg (groups B1, C1 and D1) showed no remarkable changes in the Johnsen scores as compared to the scores obtained for the vehicle

administered group (group A1) after 7 days. After 14 days of treatment, the groups of animals treated with SCS at 5, 25 and 50 mg/kg (groups B2, C2 and D2) showed a non-significant dose-dependent reduction in the scores of the spermatogenesis with a prominent decrease in the level of spermatogenesis was noted for the 50 mg/kg dose group when compared to the vehicle treated control group (group A2) (Figures 7C and 7D).

3.10 Time and dose dependent testicular toxicity evaluation of salicylidene salicylhydrazide

The testicular toxicity evaluation of mice treated with the different doses of SCS was compared with respect to the experimental time-periods of day 7 and day 14. No significant toxicological changes in the seminiferous tubules were observed on day 7 among the different treated groups. After 14 days, a variation in the testicular toxicity was noted. There was a slight increase in the toxicity for the 5 mg/kg group, while a prominent increase in toxicity was observed for the groups of SCS treated mice at 25 and 50 mg/kg doses (Figure 8A).

The testicular toxicity observed in the treated mice after day 7 and day 14 was compared with respect to the different doses of SCS i.e. 5, 25 and 25 mg/kg. The SCS treated group at 5 mg/kg has no differences in testicular changes between the tested days. For the 25 mg/kg dose, a slight increase in the toxicity was observed on day 14 as compared to day 7. The higher tested dose of 50 mg/kg showed a marked toxicological change on day 14 in comparison to changes observed on day 7 of the experiment (Figure 8B).

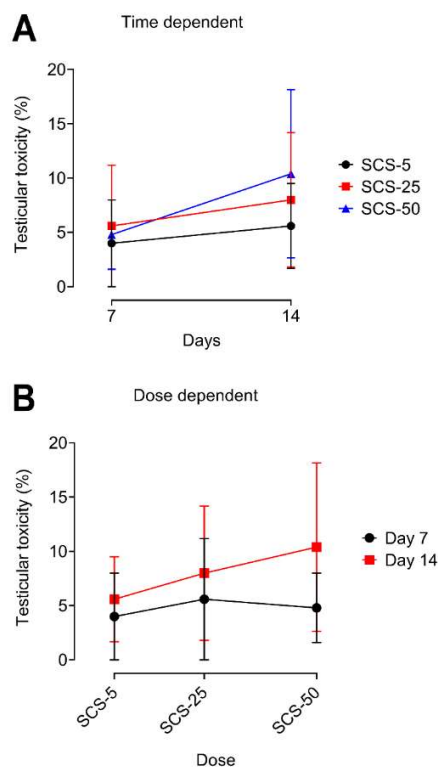


Figure 8: Time dependent (A) and dose dependent (B) testicular toxicity evaluation of salicylidene salicylhydrazide (SCS) at 5, 25, and 50 mg/kg in mice. Each symbol represents mean percentage

testicular toxicity \pm SEM. SCS groups were compared on days 7 and 14 (time dependent) or at different doses on respective days (dose dependent). No significant difference was observed, two-way repeated measures ANOVA followed by Sidak's multiple comparison *post hoc* test.

4. Discussion and conclusion

In the present study, salicylidene salicylhydrazide was assessed for its toxicological propensity in mice. The testicular tissue was evaluated for any morphological alterations occurring after repeated administration for 7 and 14 days. It was observed that the 14 days treatment with the 50 mg/kg dose produced histopathological changes in the seminiferous tubules. Exposure to the antimicrobial agent, mequindox at 55 and 110 mg/kg doses produce necrosis of the seminiferous tubules that is associated with germinal epithelium exfoliation, arresting of spermatogenesis, atrophy and disappearance of spermatogenic cells (Liu et al., 2017). The ingestion of doxorubicin at 7.5 mg/kg is associated with atrophy of the seminiferous tubules along with a loss of spermatogenic cells. It also causes vacuolization of the germinal epithelium containing multinuclear giant cells and other degenerative changes. In addition, there is also edematous changes in the interstitial tissue with a loss of interstitial cells of Leydig (Gurel et al., 2019). The degenerative changes induced by the administration of adriamycin at a dose of 10 mg/kg include reduction in the size of the germinal epithelium, formation of giant cells and thickening of the basal layer of the seminiferous tubules (Ateşşahin et al., 2006). The administration of methotrexate group at 20 mg/kg is associated with a loss of spermatogenic cells and Sertoli supporting cells from the germinal epithelium along with vacuole formation, inflammatory changes in the interstitial space and degeneration of interstitial cells of Leydig (Kamel et al., 2019). Similarly, cisplatin administration at 3 mg/kg is also associated with loss of spermatogenic cells and Sertoli cells (Prihatno et al., 2018).

In this study, the potential toxic nature of salicylidene salicylhydrazide was observed by measuring the diameter of the seminiferous tubules, thickness of the germinal epithelium and area of the Leydig interstitial cells in the different tested group. Although the low-dose and short duration (for both low and high doses) were observed to be safe with regard to the testicular histopathological changes; however, the 14 days treatment with the 50 mg/kg dose was found to have an effect on these morphometric parameters in the testicular tissue. The administration of quinine is shown to produce a gradual decline in the diameter of the seminiferous tubules after chronic dosing along with an increase in the volume of connective tissue stroma in the interstitium (Osinubi, Noronha, & Okanlawon, 2005). Chronic exposure to malathion is associated with a decrease in the germinal epithelium thickness, luminal, and tubular diameter of the seminiferous tubules (Bustos-Obregón, Del Río, & Sarabia, 2007). Cisplatin has been shown to produce significant a decrease in the seminiferous tubules diameter and an increase in the lumen diameter of tubules (Akunna et al., 2018). A significant decrease in the volume of the seminiferous tubules and an increase in the volume of the interstitium have been observed after administration of cocaine and caffeine (González et al., 2015). Administration of ribavirin also produce a decrease in the seminiferous tubular diameter and epithelial height of the seminiferous tubules (Batoool & Farzana, 2013). Moreover, dexamethasone administration has also shown to be associated with a decrease in the seminiferous tubules diameter and a reduction in the height of seminiferous germinal epithelium (Khorsandi et al., 2013). Administration of cannabis extract at doses of 40, 60 and 80 mg/kg have detrimental effect on the testis as revealed from the significant decrease in the seminiferous tubules diameter along with shrinkage of tubules (Mandal, & Das, 2010). The selenium treated animals at

a dose of 8 ppm has a considerable effect on the testicular tissue as revealed from the decrease in the diameter of the seminiferous tubules, reduction in the height of the germinal epithelium and number of spermatogenic cells (Kaur & Kaur, 2000). Likewise, ingestion of fluoride was also associated with a decrease in the epithelial height and tubular diameter of testis (Kumar & Susheela, 1995).

In this study, any testicular toxicity associated with the administration of salicylidene salicylhydrazide was investigated using modified Johnsen scoring system, which evaluates the level of spermatogenesis. The 50 mg/kg treated group was observed to produce aberrations in the spermatogenesis process after 14 days of treatment. Exposure to chemicals and drugs have been shown to produce changes in the Johnsen scoring system that are suggestive of alterations in the spermatogenesis process. The anticancer drug, cisplatin also has a toxicological propensity for the seminiferous tubules and associated with a significant decrease in the Johnsen's scores (Soni et al., 2015). The Johnsen's tubular biopsy score for the groups of animals treated with doxorubicin was significantly lowered than the control groups animals and an increase in the tubular scoring was observed after the doxorubicin animals were given a combination of zinc and alogliptin (Kabel, 2018). Application of the Johnsen's testicular biopsy scoring system to the seminiferous tubules of testes from the sildenafil, tadalafil and tramadol administered animals revealed a significant decrease in comparison to the control group after chronic administration with high doses of phosphodiesterase-5 inhibitors and tramadol (Nna et al., 2017). Similarly, the Johnsen's testicular biopsy scores were also employed to validate the underlying histopathological changes occurring in the testicular tissues in the studies conducted on cadmium (Nna et al., 2017), methyl parathion (El-Gerbed, 2013) and a significant decrease was noted in the scores after administration of these agents.

From these findings, it can be concluded that salicylidene salicylhydrazide is considered to be relatively safe. However, its absolute safety can only be established if further thorough studies are designed. These prospective controlled studies should look in-depth for the effect of salicylidene salicylhydrazide on complete semen analysis, serum concentrations of reproductive hormones including testosterone, analysis of testicular glucose, lactate and lactate dehydrogenase, assay of testicular enzymatic and non-enzymatic antioxidants and checking for markers of apoptosis in the testes. In addition, specific staining procedures for cellular apoptosis along with electron and confocal microscopic ultrastructural techniques can also be utilized.

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