



## Evaluation of the antitumor activity of *Solenostemma argel* in the treatment of lung carcinoma induced in rats

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### ABSTRACT

The present study was designed to evaluate the suspected anticancer activity of *Solenostemma argel* (200 mg/kg body weight/ day) either alone or combined with cisplatin (0.64 mg/kg body weight/day) for 4 weeks against lung cancer induced by DMBA (20 mg/kg bw) for 8 weeks in male Wistar rats. At the end of experiment, blood and Lung samples were collected to assess biochemical and biophysical markers as well histopathological investigations. *Biochemical parameters*:, serum Tumor suppressor protein (P53) and (P16), Transforming Growth Factor-beta (TGF- $\beta$ ), interleukin-1beta (IL-1 $\beta$ ), interleukin-6 (IL-6), Carcino Embryonic antigen (CEA). Lung induced nitric oxide synthase (i-Nos), cyclin dependent kinase-2 (CDK2). The level of significance between mean values was set at  $p < 0.05$ . The results of this study also showed that administration of *olenostemma argel* to lung carcinoma induced rats demonstrated a significant improvement in biochemical parameters and life span as compared to DMBA control rats. The histopathological examinations of this study revealed damage and degeneration in the lung of DMBA treated rats. Also, lung of Argel and Cisplatin rats showed significant improvement and protection against DMBA harmful effect.

**Keywords:** Cisplatin , *Solenostemma argel*, 7.12- dimethylbenz ( $\alpha$ ) anthracene.

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### 1. INTRODUCTION

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. The word tumor is abroad term to identify any growth within the body but has become synonymous with a benign or malignant growth simply; there are two types of tumors: benign or malignant .the ability to distinguish between benign and malignant is crucial in determining the appropriate treatment and

prognosis of a patient who has a tumor (Raymond, 2007).

Environmental pollutants have always been known to induce various physiological and biochemical alterations in the living system (Bouchereau et al., 1999). Among the v+ various pollutants, 7, 12-dimethylbenz ( $\alpha$ ) anthracene (DMBA) is the most potent mutagen released due to incomplete combustion (Morris and Seifter, 1992).

Cisplatin is one of the most potent chemotherapy drugs widely used for cancer treatment. The discovery of cisplatin [cis-diamminedichloroplatinum (II)] or CDDP, was a corner stone which triggered the interest in platinum (II) - and other metal-containing compounds as potential anticancer drugs. Clinical success of CDDP and its derivatives determined considerable effort to develop other effective metal-based anticancer compounds (Che and Siu, 2010). However, its use is limited due to side effects in normal tissues.

It was Barnett Rosenberg in 1965 that accidentally discovered the biological activity of *cis*-platin, which was recognized as an anticancer drug. The therapeutic activity of *cis*-platin is achieved by binding with DNA to form crosslinks as major lesions, thus inhibits replication and transcription processes and finally the cell's repair mechanism and leads to cellular apoptosis (Ali et al., 2013), (Chiavarino et al., 2015).

The plant *Solenostemma argel* (*S. argel*) belongs to the *Asclepiadaceae* family mainly located in the tropics to subtropics regions, especially in Africa and South America. It is a desert plant widely distributed in Egypt (Wadi Allaqui) with common name 'Hargal'. The plant is widely used in traditional folkloric medicine as antispasmodic [Innocenti et al., 2010], anti-inflammatory and antirheumatic agent [Shayoub et al., 2013]. Smoke inhalation and infusion of the whole plant is used in treatment of diabetes mellitus, hypercholesterolemia, jaundice, cough, cold and measles. It was described to alleviate gastrointestinal cramp, urinary tract infection and menstrual disturbance; in addition it was shown to possess anti-syphilitic properties when used for a long period of time.

This family is a rich source of indoline, alkaloids, steroids, steroidal alkaloids, pregnanes and their glycosides which possess antitumor and anticancer activities [(Si-Qi et

al., 1993) (Deepak et al., 1989)]. Previous phytochemical studies showed that the leaves are rich in carbohydrates, potassium, calcium, magnesium, and sodium while low in fibers, protein, oil, ash, copper, ferrous, manganese, and lead [Murwan and Murwa, 2010]. Moreover, investigations revealed the presence of chemical ingredients such as pyrgene glycosides, flavonoids, kaempferol, quercetin, rutin, flavonols, flavanones, chalcones and alkaloids (Shafek and Michael, 2012), (Tiagani and Ahmed, 2009), (Plaza et al., 2005). From all these ingredients, pyrgene glycosides were reported to reduce cell proliferation.

## 2. MATERIALS AND METHODS

### 2.1. Chemical compounds:

DMBA was purchased from Sigma-Aldrich Corporation (USA). *Cis*-platin (cis-PtCl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>) was obtained from Oncotec Pharma Produktion GmbH as solution for infusion in a vial of 10 mL Cisplatin Mylan (1 mg/mL).

### Preparation of *Solenostemma argel* extract

The ethanolic extract of *Solenostemma argel* was prepared according to El-Sonbaty *et al.* (2016). *Solenostemma argel* was obtained from the local market and was dried and powdered. 30 gram of plant materials were extracted by immersing them in 150 ml of the solvent for 48 hrs at room temperature under dark conditions, then filtered through clean muslin cloth followed by a filter paper, the process was repeated again for another 24 hrs. The extracts were concentrated under vacuum by rotary evaporator at 40°C. The dry extracts were stored at -80°C.

### 2.2. Experimental animals:

In all, 80 adult male Swiss albino rats (150–200 g) were obtained from the animal farm of the Egyptian Holding Company for Biological Products and Vaccines (VACSERA), Cairo, Egypt. They were maintained on a standard

pellet diet and tap water. The animals were housed in suitable cages in conditioned atmosphere (20°C–22°C) and kept on a standard diet.

### 2.3. Methods

#### *In vitro studies*

*Cytotoxicity assay using crystal violet.* A-549 cells (human cell line of a well-differentiated lung carcinoma) obtained from Egyptian National Cancer Institute, Cairo University, were used to determine the cell's cytotoxic effect of each of the tested treatments according to Mosmann, T. (1983) and Gomha et al., (2015).

#### 2.4. Experimental design:

Animals were allowed 10 days for adaptation. They were then randomly distributed into six equal groups, 15 rats each. The animal groups were recognized as follows:

1. *Group 1 (Control).* Healthy control animals.
2. *Group 2 (AR).* Animals were gavaged with Argel (200 mg/kg body weight/ day) for 4 weeks.
3. *Group 3 (cis-platin):* Each animal was injected intra-peritoneally with cisplatin at dose (0.64 mg/kg body weight/day) for 4 weeks (Medhat et al., 2017).
4. *Group 4 (DMBA):* Each animal was received DMBA intra-peritoneal injection with (20 mg/kg bw) for 8 weeks according to the modified method of Mannan et al., 2017
5. *Group 5 (AR+ cis-platin):* Rats received AR as in group 2 and *cis-platin* intra-peritoneally for 4 weeks as in group 3.
6. *Group 5 (DMBA + AR):* Rats received DMBA as in group 4 intra-peritoneal injection and then treated with AR for 4 weeks as in group 2 after induction.
7. *Group 6 (DMBA + cis-platin):* Rats received DMBA as in group 4 intra-peritoneal

injection and then treated with *cis-platin* for 4 weeks as in group 3 after induction.

8. *Group 6 (DMBA +AR+ cis-platin):* Rats received DMBA as in group 4 and then treated with AR as in group 2 and *cis-platin* for 4 weeks as in group 3 after induction.

#### *Collection of samples.*

At the end of the treatment period, animals were fasted overnight prior to dissection under light ether anesthesia. Blood was drawn from the vena cava and centrifuged at 3000g for 10 min. immediately after blood collection, lung tissue was excised and one portion was used for the histopathological examination.

The rest of the tissue was homogenized in 0.25 M ice cold isotonic sucrose to be used for the estimation of the assessed parameters

#### *Experimental parameters.*

Determination of Transforming Growth Factor-beta (TGF-β) using ELISA kits for rat (Li, et al.,2004) and serum IL-6 using ELISA kits for rat (Hirano, T. (1998), determination of CEA using Rat Carcino embryonic Antigen (CEA) ELISA Kit (Catalognumber:.MBS700529), IL-1 beta using Ray Bio® Rat IL-1 beta ELISA Kit Catalog #: ELR-IL1, P16 protein using Rat Antioncogene p16 protein (P16) Elisa kit (Competitive ELISA) Catalog Number: MBS721562, and P53 protein using Rat P53 (P53) Elisa kit Catalog Number:MBS723886.

#### *Quantitative real-time polymerase chain reaction.*

Total RNA was isolated using QIAGEN tissue extraction kit (QIAGEN, USA) according to instructions of manufacturer. Quantitative real-time polymerase chain reaction (qRT-PCR) amplification and analysis were performed using an Applied Biosystems with software version 3.1 (StepOne™, USA). The qRT-PCR assay with the primer sets was

optimized at the annealing temperature. All complementary DNAs (cDNAs) were in duplicate and included previously prepared samples for CDK2 and iNOS with glyceraldehydes 3-phosphate dehydrogenase (GAPDH) as an internal control, and water is used as non-template control to confirm the absence of DNA contamination in the reaction mixture (Table 1).

Gene symbol	Primer sequence
CDK2	5'-GCCCTAATCTCACCTCTCC-3' 5'-AAGGGTGGTGGAGGCTAACT-3'
iNOS	F: 50-CGA GGA GGC TGC CCT GCA GAC TGG-30 R: 50-CTG GGA GGA GCT GAT GGA GTA GTA-30

### 2.5. Histopathological examination:

After sacrificing the rats, lung tissue was rapidly dissected and excised, rinsed in saline solution, and cut into suitable pieces which were fixed in neutral buffered formalin (10%) for 24 h according to the method adopted by Drury and Wallington<sup>23</sup> and examined by light microscope for histopathological investigation.

### 2.6. Statistical analysis:

All statistical analyses were conducted by using the statistical package for Windows Version 15.0 (SPSS Software, Chicago, IL). The results for continuous variables were expressed as mean  $\pm$  standard error. Values were compared by one-way analysis of variance (ANOVA). Post-hoc testing was performed for inter-group comparisons using the least significant difference (LSD) test, and p values was considered statistically significant when  $p \leq 0.05$ .

## 3. RESULTS

### *In vitro studies*

The antitumor activity of Pt NPs and cisplatin was evaluated using A-549 cell lines. The chemical compounds were applied at different concentrations and results were presented in Figure 1.

### *In vivo studies*

A significant decrease in serum P53 and P16 levels were observed in DMBA induced lung carcinoma in rats compared with the normal control group.

Moreover, serum P53 and P16 levels of treatment groups were significantly increased as compared to DMBA group (Table 1).

The levels of serum TGF- $\beta$ , IL-1 $\beta$ , IL-6 and CEA of rats injection with DMBA with or without *Solenostemma argel*, cisplatin and combination between had ministration are presented in Table 1. A significant increase in serum TGF- $\beta$ , IL-1 $\beta$ , IL-6 and CEA levels were observed in DMBA induced lung carcinoma in rats compared with the normal control. Administration of *Solenostemma argel*, cisplatin and combination between after injection with DMBA induced a significant elevation in serum TGF- $\beta$ , IL-1 $\beta$ , IL-6 and CEA levels comparing to the DMBA group.

### *Quantitative real-time PCR*

Table 3 shows that the levels of i-NOs and ICDK-2 were significantly increased in lung tissue of DMBA animals as compared to control groups. However, i-NOs and ICDK-2 levels in lung of treatment groups were ameliorated as compared to DMBA animals.

Table 2. Statistical analysis (ANOVA) for serum p53, p16, TGF-β, IL-6 and CEA levels in the different groups

Groups parameters	p53 level (ng/ml)	p16 level (ng/ml)	TGF-β level (pg/ml)	IL-1β (pg/ml)	IL-6 (pg/ml)	CEA (ng/ml)
Control	27.8 ± 0.86 <sup>c</sup>	8.20 ± 0.17 <sup>c</sup>	46.30 ± 1.79 <sup>c</sup>	13.53 ± 0.38 <sup>c</sup>	33.10 ± 2.21 <sup>c</sup>	0.95 ± 0.04 <sup>c</sup>
Hargel	39.5 ± 0.98 <sup>abc</sup>	9.03 ± 0.42 <sup>c</sup>	53.37 ± 3.17 <sup>c</sup>	14.90 ± 0.75 <sup>c</sup>	26.77 ± 1.23 <sup>ac</sup>	1.01 ± 0.04 <sup>c</sup>
Cis-Platin	28.85 ± 0.95 <sup>c</sup>	8.63 ± 0.18 <sup>c</sup>	45.50 ± 1.65 <sup>c</sup>	11.70 ± 0.80 <sup>c</sup>	29.50 ± 2.14 <sup>c</sup>	0.97 ± 0.06 <sup>c</sup>
DMBA	11.17 ± 1.08 <sup>ab</sup>	2.44 ± 0.21 <sup>ab</sup>	204.70 ± 15.42 <sup>ab</sup>	126.83 ± 4.34 <sup>abc</sup>	126.20 ± 1.85 <sup>ab</sup>	4.47 ± 0.22 <sup>ab</sup>
Hargel + Cis	37.43 ± 1.41 <sup>abc</sup>	9.00 ± 0.56 <sup>c</sup>	46.97 ± 1.85 <sup>c</sup>	10.87 ± 0.35 <sup>c</sup>	29.10 ± 0.93 <sup>c</sup>	0.98 ± 0.07 <sup>c</sup>
DMBA + Hargel	19.17 ± 0.84 <sup>abc</sup>	5.10 ± 0.12 <sup>abc</sup>	100.37 ± 6.46 <sup>abc</sup>	66.77 ± 2.36 <sup>abc</sup>	53.30 ± 2.41 <sup>abc</sup>	2.17 ± 0.18 <sup>abc</sup>
DMBA + Cis	22.50 ± 1.08 <sup>abc</sup>	6.17 ± 0.32 <sup>abc</sup>	110.87 ± 5.53 <sup>abc</sup>	74.77 ± 2.41 <sup>abc</sup>	67.10 ± 2.76 <sup>abc</sup>	1.67 ± 0.09 <sup>abc</sup>
DMBA + Hargel + Cis	26.64 ± 1.34 <sup>c</sup>	7.67 ± 0.19 <sup>bc</sup>	82.43 ± 7.38 <sup>abc</sup>	29.10 ± 1.31 <sup>abc</sup>	46.70 ± 2.21 <sup>abc</sup>	1.81 ± 0.06 <sup>abc</sup>

a) Significant difference versus control group at P ≤ 0.05.

b) Significant difference versus Cis-Platin group at P ≤ 0.05.

c) Significant difference versus DMBA group at P ≤ 0.05.

Table 3. Statistical analysis (ANOVA) for lung CDK-2 and i-NOs levels in the different groups.

Groups Parameters	i-NOs level (pg/ml)	ICDK-2 (ng/ml)
Control	1.01 ± 0.01 <sup>c</sup>	1.01 ± 0.01 <sup>c</sup>
Hargel	1.01 ± 0.03 <sup>c</sup>	1.01 ± 0.01 <sup>c</sup>
Cis-Platin	1.00 ± 0.003 <sup>c</sup>	1.01 ± 0.01 <sup>c</sup>
DMBA	8.20 ± 1.08 <sup>ab</sup>	8.90 ± 0.40 <sup>ab</sup>
Hargel + Cis	1.02 ± 0.01 <sup>bc</sup>	1.00 ± 0.01 <sup>c</sup>
DMBA + Hargel	2.93 ± 0.15 <sup>abc</sup>	3.63 ± 0.32 <sup>abc</sup>
DMBA + Cis	4.00 ± 0.53 <sup>abc</sup>	3.53 ± 0.09 <sup>abc</sup>
DMBA + Hargel + Cis	1.95 ± 0.13 <sup>c</sup>	2.03 ± 0.19 <sup>abc</sup>

Legends as in Table 1.

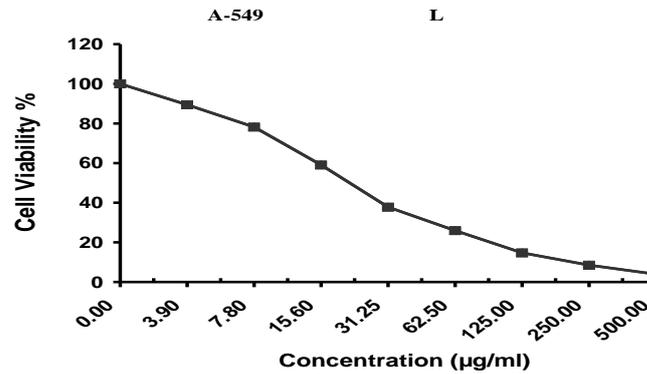


Figure 1. Cytotoxic activity of *Solenostemma argel* against A-549 cell line.

#### 4. DISCUSSION

Lung cancer is a major malignancy that affects human health. The incidence of lung cancer increases with age, and occurrence in individuals aged 55 or above is most common (Moyer 2014). Lung cancer is the third malignancy in the United States and is also a leading cause of death in patients (Moolgavkar et al., 2012).

DMBA is a polycyclic aromatic hydrocarbon used to induce breast cancer. This potent carcinogen induces DNA damage. In the cell, the reactive metabolite DMBA-3,4-dihydrodiol-1,2-epoxide (DMBA-DE) adds adenine and guanine residues to DNA. The conversion of genotoxic metabolites as DMBA-DE is promoted by the action of cytochrome P450 family. CYP1A1 and CYP1B1 are identified as the enzymes that metabolize DMBA to produce DMBA-DE (Thompson and Singh 2000).

This study was conducted to evaluate the efficiency of *Solenostemma argel* in the treatment of lung cancer either alone or combined with cis-platin both in vitro and in vivo.

In the current study, the results revealed that treated rats by intra-peritoneal injection with (20 mg/kg bw) for 8 weeks produced a

significant increase in serum p53. P53 plays a major role in preventing tumor development; it acts as a “molecular brake” to critically regulate the cell cycle. This DNA-binding protein has been involved in DNA repair and synthesis, cell proliferation, cell differentiation, programmed cell death, and in the maintenance of genomic stability mechanism (Rivlin et al., 2011). Rundle et al. (2000) reported that, the metabolic intermediates of DMBA mediate carcinogenic process by inducing the chronic inflammation through the over production of reactive oxygen species causes DNA damage. In these pathological conditions, p53 can arrest cell cycle progression, and allowing the DNA to be repaired or it can lead to apoptosis (Rundle et al., 2000). The results of the present study showed that down regulation of the p53 expression by the [6]-paradol treatment, which is in accordance with the previous reports where natural and dietary compounds have been shown to exert their chemopreventive property through modulating the balance between wild type p53 and mutant p53 protein expression (Bourdon, 2007). The results obtained in the current study showed that injection by DMBA of rats has induced a significant increase in serum TGF- $\beta$ . Transforming growth factor  $\beta$  (TGF- $\beta$ ) has a dual impact on cancer progression. In early stages of the process, it serves as a tumor suppressor, strongly inhibiting the proliferation of epithelial cells;

however, at advanced stages of the disease, it can turn into a potent driver of tumor spread and metastasis, severely worsening patient prognosis (Derynck et al. 2001; Massague 2008). Previous work has shown that the antiproliferative effect of TGF- $\beta$  is facilitated by the presence of wtp53, testifying to the cooperation of these two pivotal signaling pathways in suppression of early stages of tumor progression (Cordenonsi et al. 2003). More recent investigation of the cross talk between mutp53 and TGF- $\beta$  has revealed an intriguing duality also here. On the one hand, mutp53 can repress the expression of TGF- $\beta$  receptor type II, thereby attenuating TGF- $\beta$ -mediated signaling (Kalo et al. 2007).

A likely mechanistic explanation, although probably not the only one, is provided by the finding that the cooperation between mutp53 and TGF- $\beta$  in augmenting cell migration and metastasis is strongly enhanced by the presence of oncogenic mutant Ras (Adorno et al. 2009). Because Ras mutations are often associated with tumor progression and conversion of TGF- $\beta$  from a tumor suppressor into a prometastatic factor (reviewed in Derynck and Akhurst 2007), it is tempting to speculate that they also serve as the switch that alters the biological outcome of the interactions between mutp53 and TGF- $\beta$ .

In this study, injection of DMBA in male albino rats induced a significant increase of IL-1 $\beta$ , IL-6 and iNOS. Epidemiological studies have supported the concept that chronic inflammation frequently precedes the development of lung cancer in adults (Tockman et al., 1987). Interleukin-1beta (IL-1 $\beta$ ), a key proinflammatory cytokine encoded by the interleukin 1 beta gene, has been associated with chronic inflammation and plays an important role in lung inflammatory diseases, including lung cancer (Coussens and Werb, 2002; Ballaz and Mulshine, 2003; Smith et al., 2006). Together with tumor

necrosis factor alpha (TNF $\alpha$ ), IL-1 $\alpha$  and interleukin 1 beta are defined as “alarm cytokines” that are secreted by macrophages and initiate inflammation (Dinarello, 1996, 2002b; Apte and Voronov, 2002). Interleukin 1 alpha and Interleukin 1beta cause inflammation but more importantly they induce the expression of pro-inflammatory genes which particularly include cyclooxygenase type 2 (COX-2), inducible nitric oxide synthase (iNOS), interleukin- 6 (IL-6) and other Chemokines / cytokines (Apte et al., 2006b).

Some studies analyzed the IL-6 expression in tumor tissue, plasma and bronchoalveolar lavage, and found a correlation with progression, resistance to anti-tumor therapies and poor survival of patients with lung cancer (Chang et al., 2013, Koh et al., 2012, Matanic et al., 2003). The association between high levels of IL-6 and lower survival was also observed in patients with renal cell carcinoma (Ljungberg et al., 1997), chronic lymphocytic leukemia (Fayad et al., 1998), gastric carcinoma (Liao et al., 2008), prostate cancer (Nakashima et al., 2000), gastrointestinal cancer (De Vita et al., 2001) and breast cancer (Salgado et al., 2003).

The high IL-6 levels detected in the circulation by some suggest that these cytokine may be a marker of worse prognosis for patients with advanced NSCLC or for those treated with chemotherapy (Chang et al., 2013). Although 40% of patients with NSCLC express high concentration of IL-6, the mechanisms responsible for this correlation between IL-6 expression and poor prognosis remains to be clarified (Koh et al., 2012). Clinical and epidemiological studies suggest a strong association between chronic inflammation and some types of cancer, including NSCLC. The increased plasma levels of cytokines can act as an independent

marker of survival in patients with lung cancer.

This study showed significant decrease in CEA level in DMBA group compared to normal animals. Carcinoembryonic antigen (CEA) is a glycoprotein product of the gene CEACAM-5. It is a member of the immunoglobulin super family that serves as a cell-adhesion molecule and may also play a role in innate immunity (Hammarstrom 1999). CEA is often overexpressed in many malignant neoplasms including non-small-cell lung cancer (NSCLC) and is readily detected in serum samples making it a valuable tool for the follow-up and prognosis of patients.

A combination of epidemiologic and basic scientific evidence strongly suggests that diet and plant-derived phytochemicals may play an important role in cancer prevention or treatment (Pradeep et al., 2007a). Several mechanisms by which phytochemicals can alter carcinogenesis have been identified. Potential mechanisms include the inhibition of enzymes: modification of carcinogen detoxification through several pathways: antioxidant activities, including scavenging DNA reactive agents: suppressing abnormal proliferation of early preneoplastic lesions: and inhibiting certain properties of the cancer cell (Ceribas et al., 2010). The plant *Solenostemma argel* (*S. argel*) belongs to Asclepiadaceae family mainly located in the tropics to sub-tropic regions, especially in Africa and South America. It is a desert plant widely distributed in Egypt with common name (Hargel). The plant is widely used in traditional folkloric medicine as antispasmodic (Innocenti et al., 2010), anti-inflammatory and anti-rheumatic agent (Shayoub et al., 2013) Smoke inhalation and infusion of the whole plant is used in treatment of diabetes mellitus, hypercholesterolemia, jaundice, cough, cold

and measles. It was described to alleviate gastrointestinal cramp, urinary tract infection and menstrual disturbance, in addition it was shown to possess anti-syphilitic properties when used for a long period of time (El kamali and khalid, 1996). Sridharan et al., (2012) stated that the death of the cells might be due to the loss of mitochondria which is one the hallmarks of the apoptosis pathway. Also the difference in the antiproliferative effects between different phyto constituents and their concentrations contained in the extracts due to the sensitivity to the solvent used mode of extraction (khanapur et al., 2014).

Chemical investigations, chromatographic screening and phytochemical as well as tissue culture studies of *S. argel* leaves, stem and flowers revealed the presence of numerous biochemical ingredients and crystalline compounds and most of them were detected when extracted in alcohol such as: Pyrgene glycosides (Hassan et al., 2001 and Plaza et al., 2012), quercetin, rutin, flavanones, and alkaloids (Tigani and Ahmed, 2009).

Treatment of lung carcinoma induced rats with *S. argel* and cisplatin leads to a significant decrease in the level of serum CEA, serum Tumor suppressor protein (P53) and (P16), Transforming Growth Factor-beta (TGF- $\beta$ ), induced nitric oxide synthase (i-Nos), cyclin dependent kinase-2 (CDK2), interleukin-, interleukin-6 (IL-6), Carcino Embryonic antigen (CEA) CDK2 and a significant increase in serum Tumor suppressor protein (P53) and (P16),

## 5. Conclusion

From the aforementioned results, it can be concluded that the combined treatment of lung cancer with *S. argel* and cisplatin ameliorating the measured parameters toward normal animals and it is more potent than cisplatin or *S. argel* alone. These findings were

well appreciated with histopathological studies suggesting that *S. argel* and cisplatin can serve as a good therapeutic agent for the treatment of lung cancer which should attract further studies.

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