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# The cytotoxic effect of Vincristine-Amygdalin combination on human cervical cancer cell line (Hela cancer cell line)

Azal H. Jumaa

Department of pharmacology, College of medicine, Al Muthanna University

## Abstract:

Resistance of cancer cells toward chemotherapeutics drugs is considered as the major problem of cancer treatment. One of the strategies that are used to overcome cancer cells resistance to anticancer drugs is the drugs combination.

Vincristine and amygdalin combination was used in this study to identify the possibility of synergistic effect between them as anticancer, which is mainly due to unrelated mechanism of action for vincristine and amygdalin.

The result of the study demonstrate that the cytotoxic effect of (vincristine and amygdalin) combination was significantly more than the cytotoxicity of each one alone on Hela cancer cell line (human cervical cancer cell line). The result shows also the cytotoxicity of (vincristine and amygdalin) combination increases with the increase in the concentration which ranged between (1-10000) µg/ml, beside the increase in the incubation periods which are (24, 48 and 72) hours.

***Key word:*** *amygdalin, vincristine, Hela cancer cell line.*

## Introduction:

Medical plants have been identified and used through the history of human. Plants have the ability to synthesize many different types of chemical compounds which are useful to perform the important biological functions. There are at least 12,000 kinds of compounds have been isolated (21; 10).

A lot of recent investigations about medical Plants have been done to achieve advancements in the treatment and control of cancer progression. The main disadvantages of synthetic drugs are the associated side effects. However natural therapies, such as the use of the plants or plant derived natural products are being beneficial to kill cancer cells. Researches for anti-cancer agents from plant sources started in the 1950s.

the discovery and development of the vinca alkaloids (vinblastin and vincristine) (7), and prunus armeniaca kernels (apricot kernels) shows also a promising anticancer activity where there is several studies done to evaluate anticancer activity (5), the major role of apricot kernels anticancer effect is related to its amygdalin content.

**Corresponding address:**
**Azal H. Jumaa**
Department of pharmacology, College of medicine, Al Muthanna University
**Email:** Dr.Azalhameedy@gmail.com

Amygdalin is a glycoside, separated from the seeds of prunus dulcis, known as bitter almond. There are many different species of prunus genus such as apricot (prunus armeniaca) and black cherry (prunus serotina) contains amygdalin also (20 ), Amygdalin was reported to kill cancer cells selectively without systemic toxicity and its effect of pain relief (22), amygdalin and modified form of amygdalin (laetrile or vitamin B17) , both promoted as cancer cures (11).

Vinca alkaloids isolated from the periwinkle plant, Vinca rosea Linn. The major antitumor effect of Vincristine appears to be related to its high-affinity binding to the basic protein subunit of microtubules (tubulin), which results in disruption of the mitotic spindle apparatus and arrest of cells in metaphase, another antitumor mechanism of vincristine occurs through its ability to induce a lysosomes membrane permeabilization, causing increase leakage of lysosomes contains to the cytoplasm leading to lysis of cellular components, than cancer cells death. In addition to hydrolysis activity, the lysosomal enzymes provide acidic environment that has a role in killing tumor cells.

the capacity of lysosomes to kill cancer cells by lysosomes membrane permeabilization considered as anew development of cancer treatment (1: 6), Vincristine has been widely used in the treatment of many neoplastic diseases, including the non- Hodgkin's and Hodgkin's lymphomas, acute

lymphoblastic leukemia, breast carcinoma, Wilm's tumor, neuroblastoma (14 , 13 , 17).

**Aim of study:** the aim of study was to determine the cytotoxicity of vincristine-amygdalin combination on Hela cancer cell line in vitro.

## Material and methods:

**(amygdalin):**

Amygdalin was purchased from Santa Cruz (Santa Cruz, CA, USA) used at different concentration which ranged between (1-10000) µg/ml, these concentration achieved by dilution of amygdalin with free serum media

1. Chemotherapeutics agent;

Vincristine sulphate 1 mg/ml Injection (hospira UK.) was used at different concentration ranged between (1-10000) µg/ml, after dilution with media without serum.

**Cell culture:**

Human cervical cancer Hela cell line was purchased from tissue culture unit/ Iraqi Centre for Cancer and Medical Genetics Research (ICCMGR). The cells were cultured in 75 cm2 tissue culture flasks under humidified 5% CO2 atmosphere at 37°C in RPMI-1640 medium (Sigma chemicals, England) with 10% fetal bovine serum (FBS) provided by ICCMGR, Iraq, and penicillin- streptomycin 1% (100 U/mL penicillin and 100 µg/mL streptomycin) (Lilly, Italy) During the course of the experiment (4).

**Cytotoxicity Assay :**

Hela cancer Cells that's culture in microtiter plate (96wells) were exposed to range of concentration from (vincristine, amygdalin, (amygdalin with vincristine)), the concentration of cancer cells in each well will be increase during the log phase of growth and the cytotoxic effect of tested agents will be determined after several incubation periods. (4), every well contained 7X103cells, Serum calf medium (10%) was used for cancer cells seeding, after seeding the Plates incubated for 24hrs at 37C0 to achieve cancer cells attachment, then By using maintenance medium, fivefold serial dilution were prepared starting from (1-10000 µg/ml) for each amygdalin , vincristine and a mixture of (amygdalin with vincristine) .

After incubation for 24 hrs, cells were exposed (Six replicate at 200µl for each tested concentration), 200 µl of maintenance medium added to each well of control group, the times of exposure were 24, 48 and 72 hrs. The plates were sealed with self-adhesive film then returned to incubator, cells where staining with MTT stain.

The optical density of each well was read by using a micro-ELISA reader at a transmitting wavelength 550 nm (10; 4).

The inhibitor rate measuring by using of the following equation (5):

$$\text{Inhibitor rate \%} = \frac{\text{The optical density of control} - \text{The optical density of test.}}{\text{The optical density of control}} \times 100$$

4- Statistical Analysis :

The Statistical Analysis System (SAS) (16) was used to identify the effect of different factors in study parameters. Least significant difference –LSD test was used to compare between means in this study significantly.

## Results and discussion:

**The cytotoxic effect of vincristine:**

The growth inhibition of Hela cells that treated with vincristine increase in a dose dependant manner for each incubation periods at concentration (1, 10,100,1000,10000) µg/ml , the growth inhibition of Hela cells that treated with vincristine for 24,84 and 72 hrs. incubation periods shown in table (1) figure (1). Growth inhibition also increases at time dependent manner, where at 72 hrs. Incubation periods the growth inhibition of vincristine at concentration (10, 100 and 1000) µg/ml more than the growth inhibition of the same concentration at 24 and 48 hrs. incubation periods

**Table (1) Effect of concentration and time in growth inhibition rate for vincristine on Hela cancer cell line**

| Concentration (µg/ml) | Growth inhibition | | | LSD value |
|---|---|---|---|---|
| | 24 hr. | 48 hr. | 72 hr. | |
| 1 | C 12.00 ± 2.54 a | B 18.00 ± 2.54 a | B 20.00 ± 2.54 a | 8.791 NS |
| 10 | BC 17.00 ± 1.73 b | B 19.00 ± 1.73 b | A 36.00 ± 3.46 a | 8.476 * |
| 100 | BC 18.00 ± 4.04 b | B 23.00 ± 4.04 b | A 40.00 ± 4.04 a | 13.985 * |
| 1000 | B 24.00 ± 4.73 b | B 25.00 ± 4.73 b | A 45.00 ± 5.19 a | 16.932 * |
| 10000 | A 36.00 ± 3.17 b | A 45.00 ± 3.17 ab | A 47.00 ± 1.73 a | 9.616 * |
| LSD value | 10.758 * | 10.758 * | 11.343 * | ---- |
| * (P<0.05), NS: Non-significant. | | | | |

Different capital letter represents significant differences (P<0.05) between means of the same column; Different small letters represent significant differences (P<0.05) between means of the same row.

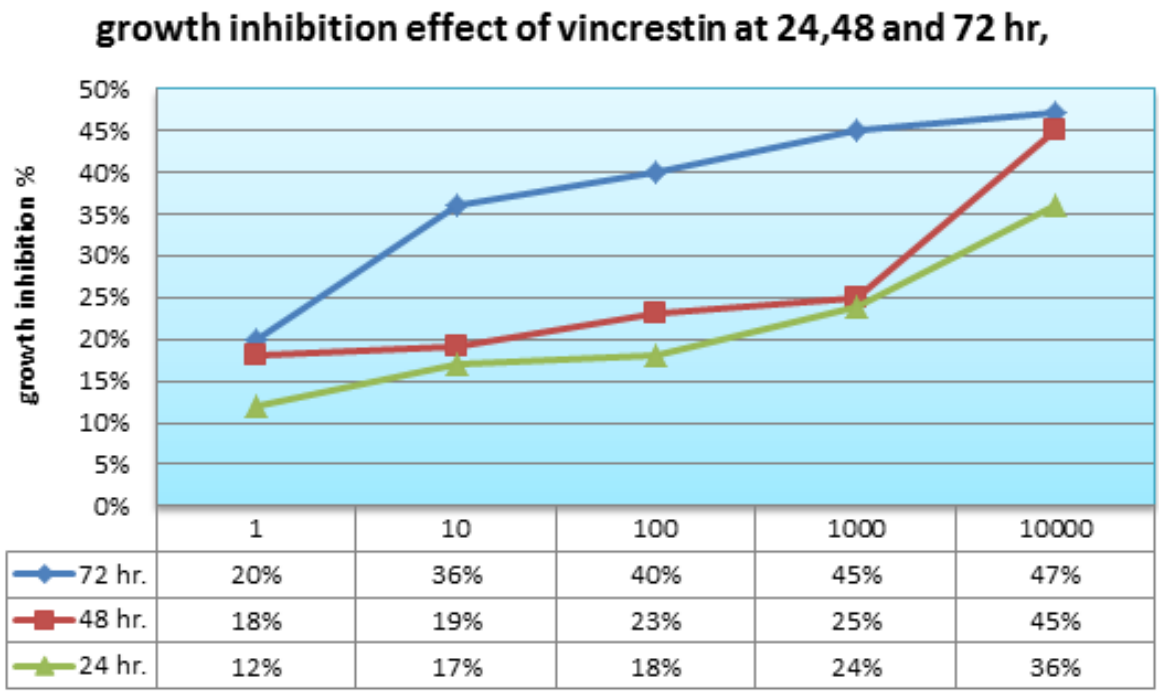



**Figure (1): Growth inhibition effect of vincristine on Hela cancer cell line**

Human cervical cancer cell line demonstrate a sensitivity to a wide range of vincristine concentration, vincristine cytotoxicity appeared dependent on both drug concentrations and the length of drug exposure, the result of vincristine cytotoxicity at 72 hr. incubation periods reflecting the mechanism of its action including an increase in its cytotoxicity occurs with increase in its time of persistence inside the cancer cells, which related to the ability of vincristine to forming a crystal forming of microtubules in 28 lymphoid malignancy with a different percentage of cells showing microtubules changes and progression significantly with increase in the duration of exposure , A similar data shown in another study concluded a progression reduction in murine leukemia survival and a suppression of human lymphoblastoid leukemia cells occurred with increase in the concentration of vincristine (14 ; 7 ; 3) .

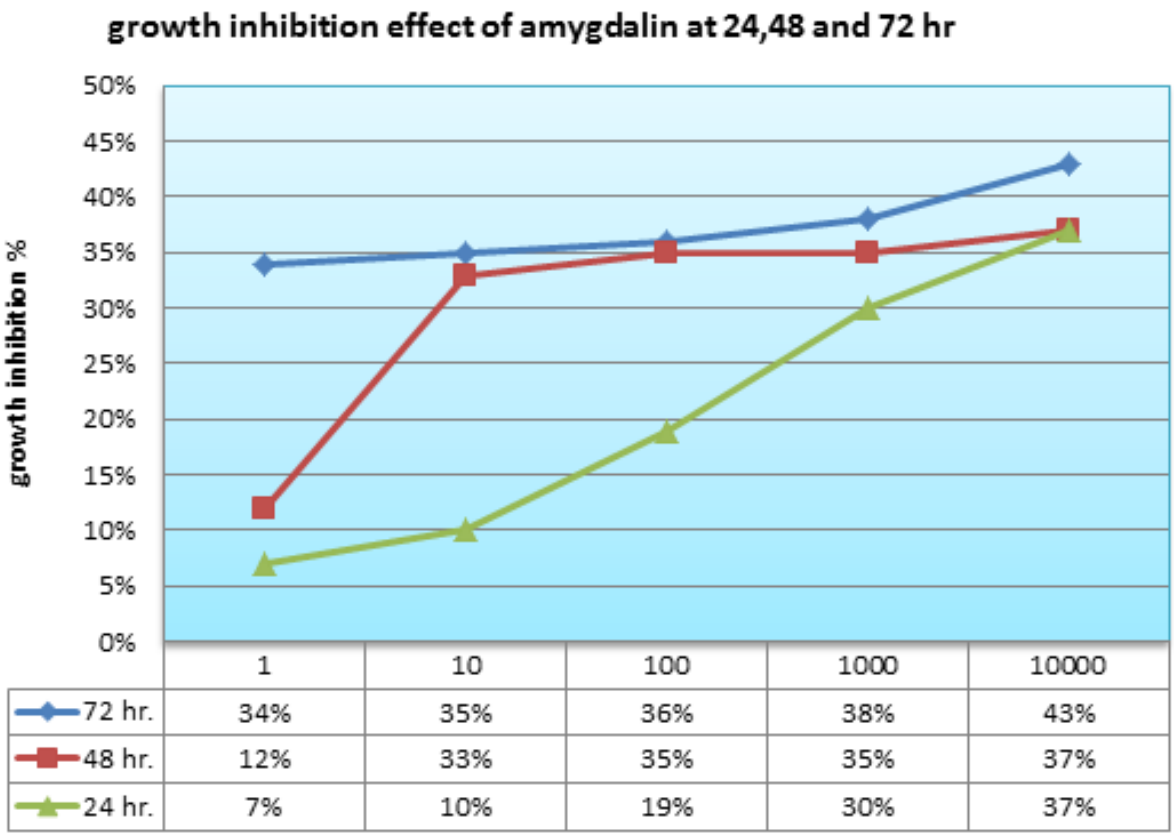
**The cytotoxic effect of amygdalin:**

The result demonstrates a dose dependent manner was the style of Hela cell growth inhibition that treated with amygdalin in all incubation periods specially at 24 hr. Incubation period. growth inhibition of Hela cells show also time dependent manner especially at 72 hr. incubation periods compared with 24 and 48 hr. incubation periods for all amygdalin concentration (table 2, figure 2) .

**Table (2) Effect of concentration and time in growth inhibition rate for Amygdalin on Hela cancer cell line**

| Concentration (µg/ml) | Growth inhibition | | | LSD value |
|---|---|---|---|---|
| | 24 hr. | 48 hr. | 72 hr. | |
| 1 | D 7.00 ± 2.54 b | B 12.00 ± 2.54 b | A 34.00 ± 2.54 a | 8.791 * |
| 10 | CD 10.00 3.46 b | A 33.00 ± 1.73 a | A 35.00 ± 1.73 a | 8.476 * |
| 100 | BC 19.00 ± 4.04 b | A 35.00 ± 4.04 a | A 36.00 ± 4.04 a | 13.985 * |
| 1000 | AB 30.00 ± 5.19 a | A 35.00 ± 4.73 a | A 38.00 ± 4.73 a | 16.932 NS |
| 10000 | A 37.00 ± 1.73 a | A 37.00 ± 3.17 a | A 43.00 ± 3.17 a | 9.616 NS |
| LSD value | 11.343 * | 10.758 * | 10.758 NS | ---- |
| * (P<0.05) , NS: Non-significant. | | | | |

Different capital letter represents significant differences (P<0.05) between means of the same column; Different small letters represent significant differences (P<0.05) between means of the same row.




| | 1 | 10 | 100 | 1000 | 10000 |
|---|---|---|---|---|---|
| 72 hr. | 34% | 35% | 36% | 38% | 43% |
| 48 hr. | 12% | 33% | 35% | 35% | 37% |
| 24 hr. | 7% | 10% | 19% | 30% | 37% |

**Figure (2): Growth inhibition effect of Amygdalin on Hela cancer cell line**

Amygdalin show an increase in their cytotoxicity toward Hela cancer cell line with increase in the amygdalin concentration and duration of exposure (concentration and time depends) , this cytotoxicity mainly related to the effect of hydrocyanic acid and benzaldehyde that liberated inside the cancer calls under the analytical effect of glucosidase enzyme (11) .

The antineoplastic effect of hydrocyanic acid occurs through its ability to inhibition of cytochrome C oxidase in the respiratory electron transport chain of the mitochondria, impairing both oxidative metabolism and the associated process of oxidative phosphorylation, eventually causing energy deprivation (12), while benzaldehyde cytotoxicity occurs through its ability to induce apoptosis by caspase 3,8 and 9 activation (21) . amygdalin by depending on dose and time of exposure have ability to induce apoptosis by caspase-3 activation through downregulation of antiapoptotic Bcl-2 protein and up regulator of proapoptotic Bax protein in prostate cancer cells (2).

**The cytotoxic effect of mixture:**

The growth inhibition result of the mixture shown a similar pattern of Hela cell growth inhibition effect of vincristine and amygdalin through their ability to induce growth inhibition by a concentration and time dependent, where these result demonstrate the growth inhibition of the mixture increase with increase in the mixture concentration which ranged between (1-10000) µg/ml, also increase with increase in the incubation periods especially at 72 hr. incubation periods, at this incubation period the mode of combination between the mixture component was synergistic as seen in combination index ,table (5,7,9) and figure (5,7,9), When comparing the growth inhibition effect among the mixture, amygdalin and vincristine for 24, 48 band 72 hr. as shown in table (4, 6 , 8) figure (4,6 , 8) , the growth inhibition effect of the mixture at 10000 µg/ml at 24 , 48 and 72 hr. significantly was more than the growth inhibition of vincristine and amygdalin alone at the same concentration .

The style of mixture component combination between (vincristine and amygdalin) was synergetic at concentration 1µg of mixture in 24hr. and at (1µg, 10000 µg) in 48hr. while at 72hr. incubation period all the concentration of the mixture show a synergisms pattern of combination as shown in table (5,7,9) and figure (5,7,9), the pattern of combination can be concluded after comparing the combination index value of each concentration at three incubation period with the guideline combination index value table (10) (19).

**Table (3) Effect of concentration and time in growth inhibition rate for a mixture of amygdalin and vincristine on Hela cancer cell line**

| Concentration (µg/ml) | Growth inhibition | | | LSD value |
|---|---|---|---|---|
| | 24 hr. | 48 hr. | 72 hr. | |
| 1 | D 17.00 ± 2.54 c | B 28.00 ± 2.54 b | C 43.00 ± 2.54 a | 8.791 * |
| 10 | CD 22.00 ± 3.46 c | B 34.00 ± 1.73 b | C 49.00 ± 1.73 a | 8.476 * |
| 100 | BC 31.00 ± 4.04 b | B 35.00 ± 4.04 b | C 53.00 ± 4.04 a | 13.985 * |
| 1000 | B 35.00 ± 5.19 b | B 38.00 ± 4.73 b | B 64.00 ± 4.73 a | 16.932 * |
| 10000 | A 57.00 ± 1.73 b | A 59.00 ± 3.17 b | A 75.00 ± 3.17 a | 9.616 * |
| LSD value | 11.343 * | 10.758 * | 10.758 * | ---- |
| * (P<0.05). | | | | |

Different capital letter represents significant differences (P<0.05) between means of the same column; Different small letters represent significant differences (P<0.05) between means of the same row.

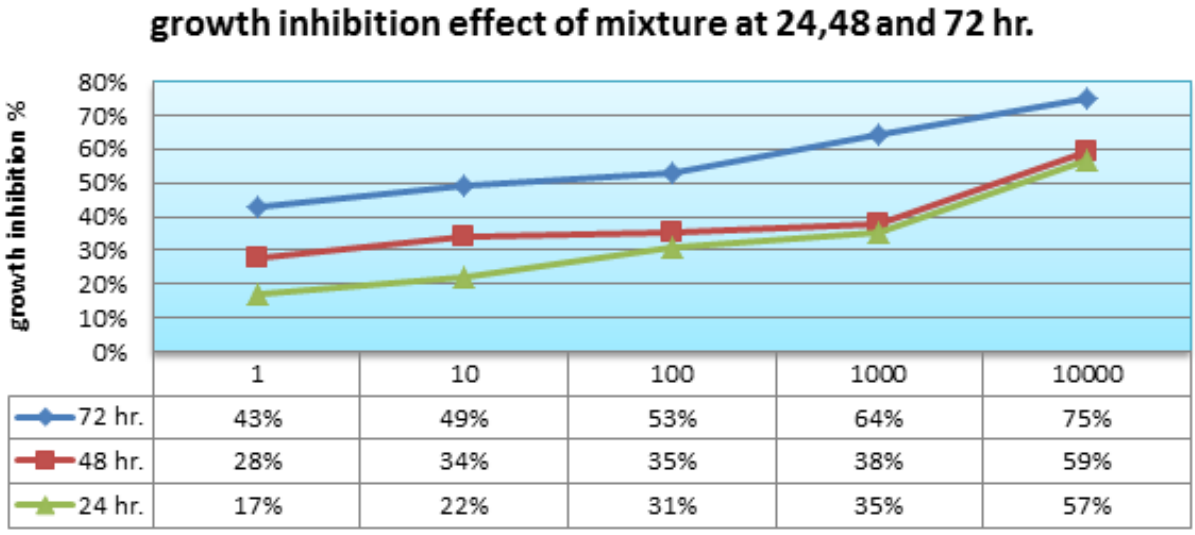



**Figure (3): Growth inhibition effect of mixture on Hela cancer cell line**

Mixture growth inhibition related to the cytotoxicity of vincristine and amygdalin plus the sharing potentiation ability between them including the ability of vincristine to enhance the cytotoxicity of amygdalin, plus the ability of amygdalin to minimize the resistance of Hela cancer cells to the vincristine cytotoxic effect.

Amygdalin anticancer activity mainly depends on the cytoplasmic level of cyanide and benzaldehyde that librated from amygdalin decomposition by the analytical effect of glucosidase enzyme. therefore glucosidase consider as the key role for amygdalin cytotoxicity , agents that have ability to increase the availability of glucosidase enzyme intracellularly causing paradoxically to increase amygdalin cytotoxicity , vincristine play a role for increase amygdalin cytotoxicity through its ability to provides more glucosidase enzyme, that's done through vincristine ability to induce lysosomes membrane permeabilization leading to availability of more glucosidase enzyme in the cytoplasm which is one of different lysosomal hydrolytic enzymes contains in lysosomes (1; 6 ; 8) .

Another suggested potentiation mechanism between the mixture contains including the ability of cyanide that liberated from amygdalin decomposition inside cancer cells to minimized the resistance of cancer cells toward vincristine cytotoxicity , and that occurs through the ability of cyanide to induce energy deprivation(12) , causing lowering of essential ATP level that's need to maintenance the normal function of P- glycoprotein transporting system (it's an ATP-dependent efflux pump) , which responsible for efflux of vincristine outside the cancer cells (20) .

Energy deprivation by the action of cyanide also minimize the development of cancer cells resistance against ability of vincristine to lysosomes membrane permeabilization action, through minimized the Hsp70 family of chaperones protein overexpression in cancer cells (9 ) , by minimized the level of ATP that essential for Hsp70 family of chaperones protein overexpression.

By Decreasing in the expression of Hsp-70 chaperone protein, the resistance development would be minimized, by minimize the resistance ability of lysosomes membrane to the lysosomes acidic media (15), causing increase in the permeability of lysosomal membrane than eventually leakage of lysosomes contains to the cytoplasm of cancer cell.

Mixture ability to induce apoptosis occur by two divers pathways, fist; through the ability of benzaldehyde that liberated from amygdalin decomposition to induce apoptosis by activation of caspase 3.8 and 9 (18), second one included the ability of vincristine to provokes the translocation of lysosomal contents to the cytoplasm, including proteases that implicated in cell death by cathepsin B, CD, and cathepsin L , These proteases trigger a cascade of events culminating in the activation of apoptotic effectors, including mitochondria, caspases, and other as yet- unknown effectors (1).

**Table (4): Growth Inhibition Effect of Vincristine, Amygdalin and (Vincristine and Amygdalin) 24hr.**

| Concentration (µg/ml) | Growth inhibition | | | LSD value |
|---|---|---|---|---|
| | Mix. | AMYG. | Vin. | |
| 1 | D 17.00 ± 2.54 a | D 7.00 ± 2.31 b | C 12.00 ± 2.54 ab | 8.532 * |
| 10 | CD 22.00 ± 1.73 a | CD 10.00 ± 4.67 a | BC 17.00 ± 3.46 a | 12.131 NS |
| 100 | BC 31.00 ± 4.04 a | BC 19.00 ± 1.67 b | BC 18.00 ± 4.04 b | 11.899 * |
| 1000 | B 35.00 ± 4.73 a | AB 30.00 ± 4.04 a | B 24.00 ± 5.19 a | 16.200 NS |
| 10000 | A 57.00 ± 3.17 a | A 37.00 ± 2.31 b | A 36.00 ± 1.73 b | 8.573 * |
| LSD value | 10.758 * | 10.13 * | 11.343 * | ---- |
| * (P<0.05), NS: Non-significant. | | | | |

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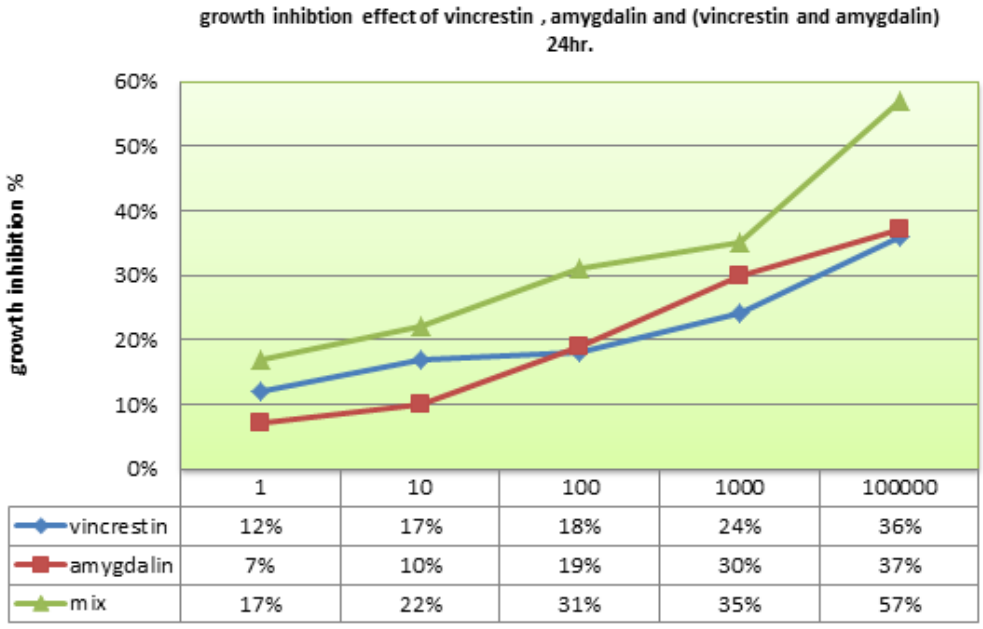


**Figure (4): Growth inhibition of Vincristine, Amygdalin and (Vincristine and Amygdalin) 24hr**

**Table (5); Combination index value for mixture at 24hr. incubation period**

| Total mixture Dose | Combination index Value | Pattern of combination |
|---|---|---|
| **µg/ml 2** | 0.64492 | synergism |
| **µg/ml 20** | 1.09394 | Nearly additive |
| **µg/ml 200** | 1.76434 | Antagonism |
| **µg/ml 2000** | 2.66775 | Antagonism |
| **µg/ml 20000** | 9.51184 | Strong Antagonism |

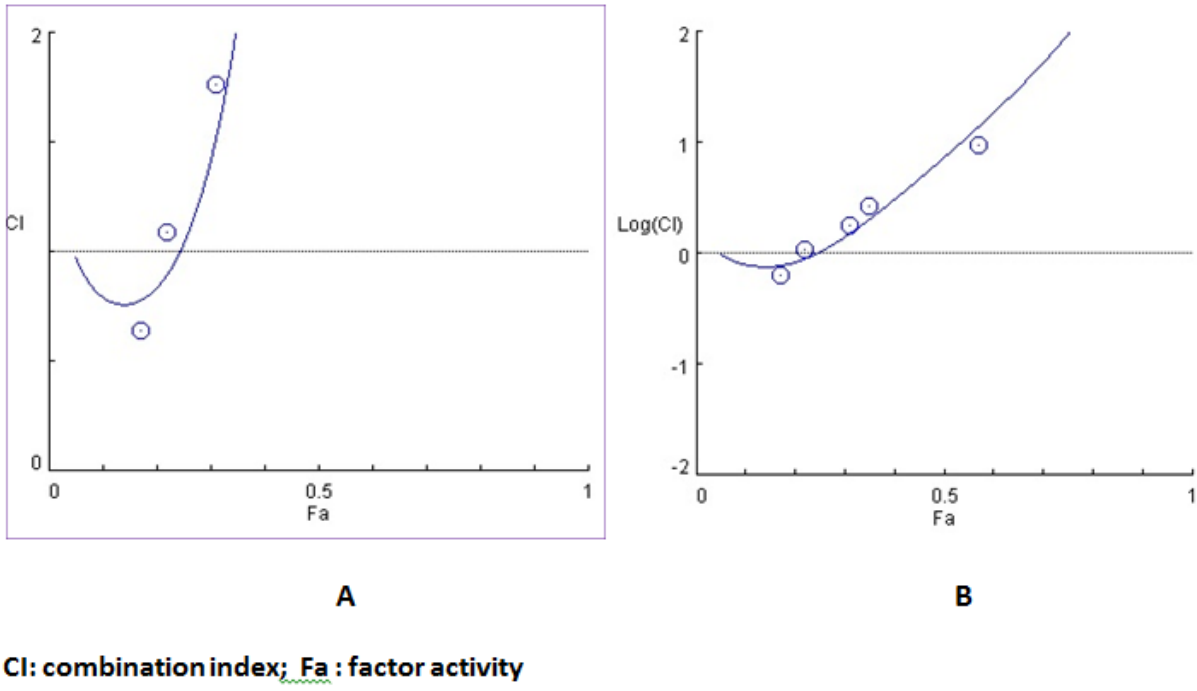


**Figure (5): A combination index plot; B logarithmic combination index plot for mixture at 42hr. incubation period (CI < 1 indicates Synergism, CI = 1 indicates Additive Effect, CI > 1 indicates Antagonism) ,(Ting-Chao & Martin , 2004).**

**Figure (6): Growth inhibition of Vincristine, Amygdalin and (Vincristine and Amygdalin) 48hr.**

| Concentration (µg/ml) | Group | | | LSD value |
|---|---|---|---|---|
| | Vin. | AMYG. | Mix | |
| 1 | B 18.00 ± 2.54 b | B 12.00 ± 2.54 b | B 28.00 ± 2.54 a | 8.791 * |
| 10 | B 19.00 ± 1.73 b | A 33.00 ± 1.73 a | B 34.00 ± 3.46 a | 8.476 * |
| 100 | B 23.00 ± 4.04 a | A 35.00 ± 4.04 a | B 35.00 ± 4.04 a | 13.985 NS |
| 1000 | B 25.00 ± 4.73 a | A 35.00 ± 4.73 a | B 38.00 ± 5.19 a | 16.932 NS |
| 10000 | A 45.00 ± 3.17 | A 37.00 ± 1.73 | A 59.00 ± 1.73 | 9.616 * |
| LSD value | 10.758 * | 10.758 * | 11.343 * | ---- |
| * (P<0.05) , NS: Non-significant. | | | | |

Different capital letter represents significant differences (P<0.05) between means of the same column; Different small letters represent significant differences (P<0.05) between means of the same row.

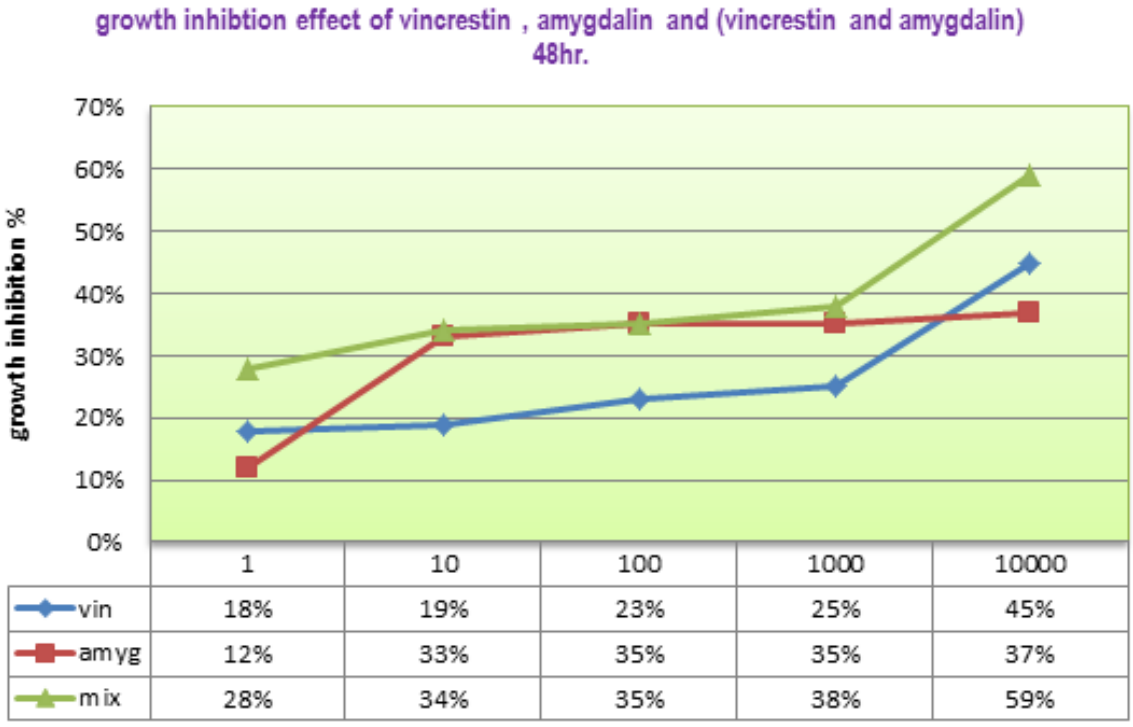


**Figure (6): Growth inhibition of Vincristine, Amygdalin and (Vincristine and Amygdalin) 48hr.**

**Table (7); Combination index value for mixture at 48hr. incubation period**

| Total mixture Dose | Combination index Value | Pattern of combination |
|---|---|---|
| **µg/ml 2** | 0.71230 | Moderate synergism |
| **µg/ml 20** | 0.98603 | Nearly additive |
| **µg/ml 200** | 1.39614 | Moderate antagonism |
| **µg/ml 2000** | 1.57294 | antagonism |
| **µg/ml 20000** | 0.65615 | synergism |

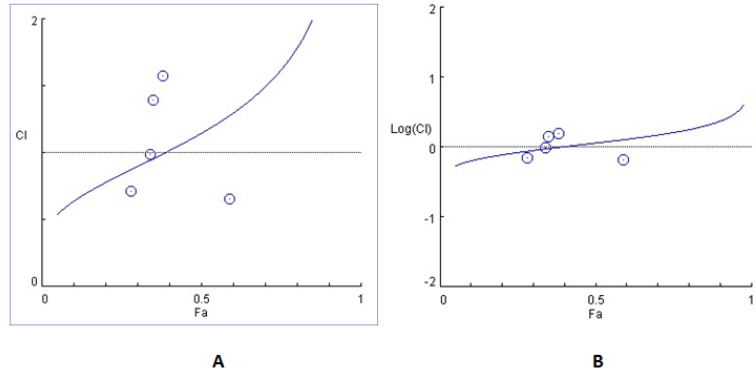


**Figure (7): A combination index plot; B logarithmic combination index plot for mixture at 48hr. incubation period ;( CI < 1 indicates Synergism, CI = 1 indicates Additive Effect, CI > 1 indicates Antagonism) (Ting-Chao & Martin , 2004).**

**Table (8): Growth Inhibition Effect of Vincristine, Amygdalin and (Vincristine and Amygdalin) 72hr.**

| Concentration (µg/ml) | Group inhibition | | | LSD value |
|---|---|---|---|---|
| | Vin. | AMYG. | Mix | |
| 1 | B 20.00 ± 2.54 c | A 34.00 ± 2.54 b | C 43.00 ± 2.54 a | 8.791 * |
| 10 | A 36.00 ± 3.46 b | A 35.00 ± 1.73 b | C 49.00 ± 1.73 a | 8.476 * |
| 100 | A 40.00 ± 4.4 ab | A 36.00 ± 4.04 b | C 53.00 ± 4.04 a | 13.985 * |
| 1000 | A 45.00 ± 5.19 b | A 38.00 ± 4.73 b | B 64.00 ± 4.73 a | 16.932 * |
| 10000 | A 47.00 ± 1.73 b | A 43.00 ± 3.17 b | A 75.00 ± 3.17 a | 9.616 * |
| LSD value | 11.343 * | 10.758 NS | 10.758 * | ---- |
| * (P<0.05) , NS: Non-significant. | | | | |

Different capital letter represents significant differences (P<0.05) between means of the same column; Different small letters represent significant differences (P<0.05) between means of the same row.

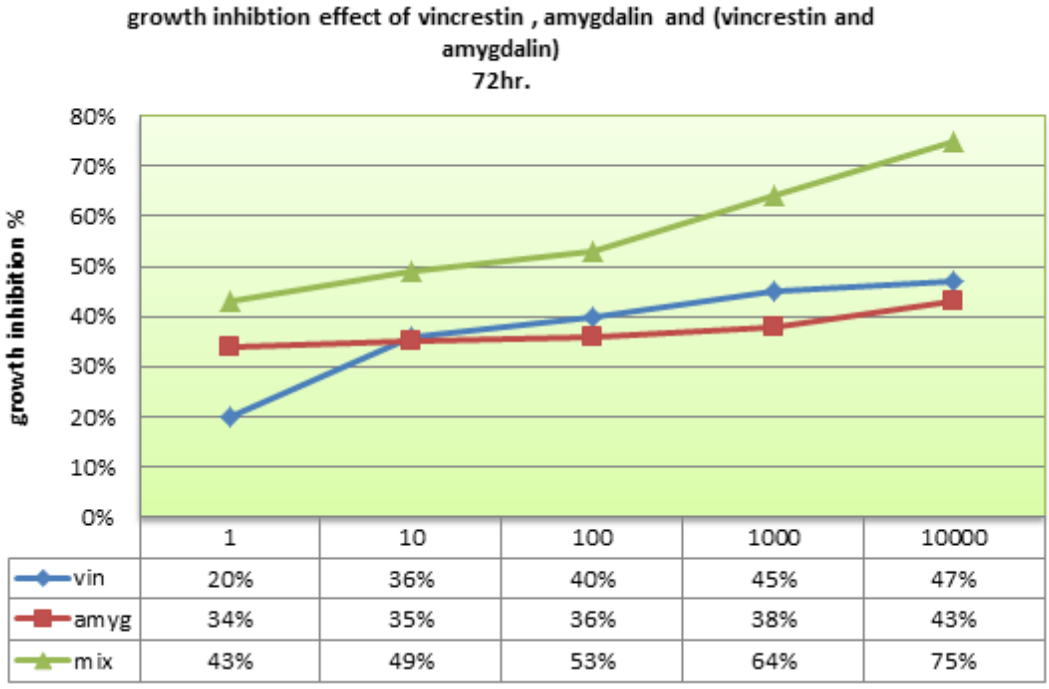


**Figure (8): Growth inhibition of Vincristine, Amygdalin and (Vincristine and Amygdalin) 72hr.**

**Table (9); Combination index value for mixture at 72hr. incubation period**

| Total mixture Dose | Combination index Value | Pattern of combination |
|---|---|---|
| **µg/ml 2** | 0.39007 | synergism |
| **µg/ml 20** | 0.47324 | synergism |
| **µg/ml 200** | 0.54072 | synergism |
| **µg/ml 2000** | 0.37400 | synergism |
| **µg/ml 20000** | 0.23529 | Strong synergism |

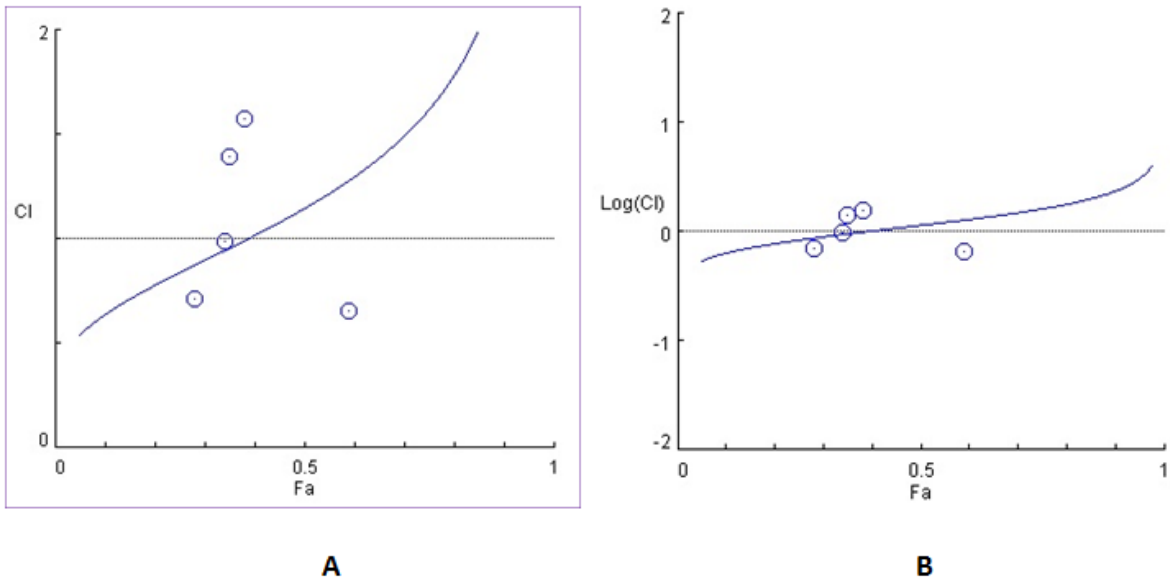


**Figure (9): A combination index plot; B logarithmic combination index plot for mixture at 72 hr. incubation period ;( CI < 1 indicates Synergism, CI = 1 indicates Additive Effect, CI > 1 indicates Antagonism) (Ting-Chao & Martin , 2004).**

**Table (10); guideline for determine pattern of Synergism and Antagonism by using Combination index analysis,(Ting-Chao & Martin , 2004).**

| Combination index | Pattern of combination |
|---|---|
| 0.1 > | Very Strong Synergism |
| 0.3–0.1 | Strong Synergism |
| 0.7–0.3 | Synergism |
| 0.85–0.7 | Moderate Synergism |
| 0.90–0.85 | Slight Synergism |
| 1.10–0.90 | Nearly Additive |
| 1.20–1.10 | Slight Antagonism |
| 1.45–1.20 | Moderate Antagonism |
| 3.3–1.45 | Antagonism |
| 10–3.3 | Strong Antagonism |
| 10 < | Very Strong Antagonism |

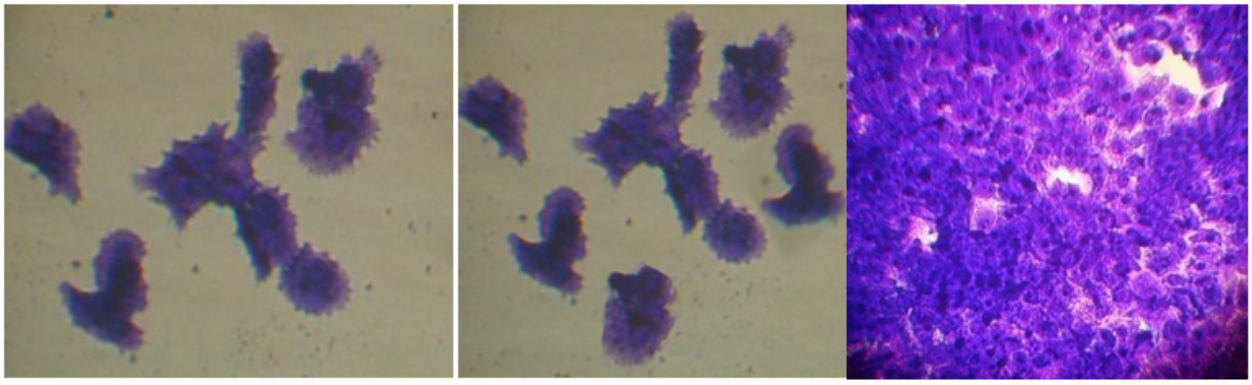


**Figure (10): Morphology of the HeLa cells. (A & B) HeLa cells treated with 10000 (µg/ml) of (Vincristine and Amygdalin) at 72hr, showing feathering formation (arrow head), loss of polarity and the nuclei are crowded hyperchromasia (arrow). (C) The HeLa cells for control groups, without any treatments, showing a cluster of neoplastic cells, showed a tightly packed with scant cytoplasm, finely granular nuclear chromatin (arrow) and nucleoli are absent.**

**Conclusion:**

The result of this study demonstrate that the combination of (amygdalin , vincristine) has ability to inhibit the growth of human cervical cancer cells in vitro by a suggested mechanism including a potentiation ability of vincristine to the cytotoxicity of amygdalin on Hela cells , and the ability of amygdalin to minimized the development of Hela cancer cells resistance to vincristine activity .

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# التأثير السمي الخلوي لمزيج (ألأمكدالين و الفنكرستيين) على خط خلايا سرطان عنق الرحم البشري Hela

أزل حمودي جمعة

فرع الادوية، كلية الطب، جامعة المثنى.

**الخلاصه:**

تعتبر مقاومة الخلايا السرطانية للعلاجات الكيمياوية المضادة للسرطان احدى اكبر المشاكل التي تؤدي الى فشل عمل تللك العلاجات , حيث استخدمت اكثر من استراتيجية لتقليل مقاومة الخلايا السرطانية لعمل العلاجات الكيماوية و من تللك الاستراتجيات استخدام مزيج متكون من اكثر من علاج كيمياوي واحد.

لقد استخدمت في الدراسة الحالية مزيج ( الامكدالين مع الفنكرستيين) وذلك لاجل تقييم التأثير السمي الخلوي التأزري لمكونات المزيج على نمو خلايا سرطان عنق الرحم البشري Hela))

اظهرت نتائج الدراسة ان التأثير السمي الخلوي لمزيج (الامكدالين مع الفنكرستيين) كان اكثر معنويا من التأثير السمي الخلوي لكل من الامكدالين و الفنكرستيين كل على حدة على نمو خط خلايا سرطان Hela .

وأظرت النتائج ايضا ان التأثير السمي الخلوي لمزيج ( الامكدالين و الفنكرستيين) قد أزداد مع ازدياد تراكيز المزيج و التي تراوحت مابين (10000-1) مايكروغرام / ملل , مع ازدياد السمية الخلوية للمزيج مع ازدياد اوقات الحضن والتي كانت (24, 48,72) ساعة .

**الكلمات المفتاحية :** الامكدالين , الفنكرستيين , خط خلايا سرطان عنق الرحم البشري ((Hela