INTRODUCTION
The new compound [5- chloro -2- (methyl sulfanyl) pyrimidine -4- amine] cobalt (II) complex, show an anti oxidant activity in vivo and in vitro studies. So for more investigation activity of this compound on metastasis of chromosomes, we are carrying out this experiment. Mitosis is a controlled series of events in which identical copies of the genome are moved to the two poles of a mitotic spindle that eventually become nuclei of the resulting daughter cells. Since uncontrolled and rapid cell division is a hallmark of cancer, understanding the molecular mechanism underling mitosis is key to understanding how various natural product anti mitotic agents function. Whereas the vinca alkaloids were originally identified as compounds that arrested cells in mitosis with aberrant mitotic spindles. Compounds such as colchicines had been known to possess an anti mitotic activity for decades. Microtubules are extremely important in the process of mitosis, during which the duplicated chromosomes of a cell are separated into two identical sets before cleavage of the cell into two daughter cells. Their importance in mitosis and cell division makes microtubules an important target for anticancer drugs. Microtubules and their dynamics are the targets of a chemically diverse group of anti mitotic drugs (with various tubuline-binding sites) that have been used with great success in the treatment of cancer. In view of the success of this class of drugs, it has been argued that microtubules represent the best cancer target to be identified so far, and it seems likely that drugs of this class will continue to be important chemotherapeutic agents, even as more selective approaches are developed. Microtubules seem to be a favorite target of naturally occurring presumably self-protective, toxic molecules that are produced by a large number of plants and animals ranging from algae to sea hares and most microtubule-targeted compounds have been discovered in largescale screens of natural products. These were serendipitously discovered to exert bone marrow toxicity during the investigation of their reputed anti diabetic activity in folk medicine. The biological functions of microtubules in all cells are determined and regulated in large part by their polymerization dynamics. Microtubules show two kinds of non-equilibrium dynamics, both with purified microtubule systems in vitro and in cells. One kind of dynamic behavior that is highly prominent in cells, called ‘dynamic instability’ is a process in which the individual microtubule ends switch between phases of growth and shortening. The two ends of a microtubule are not equivalent; one end, called the plus end grows and shortens more rapidly and more extensively than the other (the minus end). The changes

ABSTRACT
Colchicines inhibit microtubule polymerization by binding to tubulin, one of the main constituent microtubules. The mitosis inhibiting activity of colchicines has been of great use in the study of cellular genetic. The Aim of this study is to investigate the mitotic inhibitor activity of [6- chloro-2- (methyl sulfanyl) pyrimidine -4- amine] cobalt (II) complex, in vivo study. A treatment with cobalt(II) complex of pyrimidine derivative caused a significant reduction in the metaphase index 43% as compared to the colchicines 88%.
in length with time at the ends of a group of microtubules due to dynamic instability are illustrated in Figures (1-3). The microtubules undergo relatively long periods of slow lengthening brief periods of rapid shortening and periods of attenuated dynamics or pause, when the microtubules neither grow nor shorten detectably. Despite the success of the tubulin-targeting agents, the therapeutic potential of this class of compound is limited by the fact that many rapidly dividing cell types are required for normal physiological function. In normal cells, microtubules are responsible for a variety of functions like cell shape, cell motility, signal transduction, intracellular transport and muscle contractions. Many tubulin-targeting drugs are known to cause neurotoxicity through their ability to interfere with the function of axonal microtubules that mediate neuronal vesicle transport. Another drawback of tubulin-targeting drugs is their lack in efficacy in many settings. For example, although paclitaxel is one of the most broadly active anti-tumor agents, the majority of patients with advanced disease do not enter long-term remission. The resistance to the drugs is developed because of drug efflux pumps and alterations in tubulin functions. The vinca alkaloids and taxanes are both good substrates for the 170 kDa P-glycoprotein (Pgp) efflux pump encoded by the multidrug resistance mdr1 gene. The Aim of this study is to investigate the mitotic inhibitor activity of [6-chloro-2-(methyl sulfanyl) pyrimidine-4-amine] cobalt(II) complex, in vivostudy.

MATERIAL AND METHODS
Cytogenetic toxicity in bone marrow.

Used solutions
The following solutions were prepared according to Yaseen, 1990.

1- Colchicines Solution
Colchicines solution was prepared by dissolving one colchicine tablet (1mg of crystallized colchicines) in 10 ml distilled water. The solution was filtered and, then it was stored at 4°C for four days as a maximum.

2- Hypotonic solution(0.075M KCl)
The solution was prepared by dissolving 1.1175 g of KCl powder in 200 ml of distilled water; the stock solution was stored at 4°C until used for cytogenetic study 13.

3- The fixative solution
It was employed for cytogenetic studies, freshly made mixture of absolute methanol and glacial acetic acid in the ratio 3:1 (V/V) for cytogenetic study 13.

A - Direct methods
The protocol of (Allen et al) was done to study with some modification as follow:

1. Skin and muscle tissues were removed from both femurs immediately after sacrifice. Both epicondyle tips were removed with scissors, and the marrow expelled, using a syringe with a 24-gauge needle with 5ml of warm sterile PBS until the bone being clear, into a centrifuge tube. The suspension was mixed well to assure dissociation of the cells.

2. The cell suspension was treated with 0.1ml colchicine at 37°C for 20 minutes.

3. The cell were centrifuged at 1500 rpm for 10 minutes and the supernatant was discarded.

4. Five ml of 37°C hypotonic solution (warmed KCl) was added the cell pellet and the suspension mixed thoroughly. The cells were incubated at 37°C in a water bath for 30 minutes.

5. The cells were centrifuged at 1500 rpm for 10 minutes and the supernatant was discarded.

6. Freezer-chilled, freshly prepared fixative methanol: glacial acetic acid (3:1) was added drop-wise, with initial mixing, to give a total volume of 5ml. The cells were gently resuspended and then refrigerated at 4°C for one hour.

7. The cells were centrifuged at 1500 rpm for 10 minutes and the supernatant was discarded.

8. Five ml of fresh fixative was added, cells resuspended and centrifuged at 1500 rpm for 10 minutes. Two other consecutive washes with the fixative were made. One ml of the fixative was added to the cells after the last wash.
B - Slide Preparation and Staining

The cells were resuspended and then dropped from a height of about 0.5 meter, using a Pasteur pipette onto wet, chilled, grease-free slides and allowed to dry at room temperature. The slides were stained with freshly prepared Giemsa stain (1 volume Giemsa stain stock and 4 volume Sorenson’s buffer) for 2 minutes, then washed with Sorenson’s buffer and left to dry at room temperature [13]. Microscopic examination under 100X objective lens was performed to determine the mitotic index (MI%) and blast index (BI%).

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\text{MI} = \frac{\text{Number of chromosomal metaphase} \times 100}{1000}
\]

\[
\text{BI} = \frac{\text{Number of blastocytes} \times 100}{1000}
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RESULTS AND DISCUSSION

In the present study, an only cell at metaphase were scored in samples of bone marrow and there for the metaphase index were based on the percentage of these cells show in Table (1). A treatment with Cobalt (II) complex of pyrimidine derivative caused a significant reduction in the metaphase index 43% as compared to the Colchicines 88%, this result in agree with (Chang, 1995)\textsuperscript{15}. This data involved the following structural chromosome aberrations after treatment with cobalt (II) complex of pyrimidine derivative. This abnormality indicates the absence or loss of a segment at the end of one chromatid or one of a chromosome as a deletion, as perceived in Figures (1-3) from the statistical view the highest mean value of deletions. The Centromeric Attenuation another aberration. This case is marked by the fact that the centromere of a chromosome is inclined to either stretching or splitting. In the former instance, the two chromatids join together by a very thin chromatin thread, as observed in Figure s(1-3),the two chromatids are completely separated from each other. The Fragments of the other chromosome are aberrations. In this aberration, the metaphase spread involves one or more chromosomes in fragmented appearance. However, some chromosomes in this abnormality occurred in centric or a centric type, as represented in Figures (1-3). This result agreement with (Naglaet al., 2013)\textsuperscript{16}, but our result disagreement with (Epstein, 1984)\textsuperscript{17}, which show the ring chromosome.

<table>
<thead>
<tr>
<th>Cell division</th>
<th>Colchicines /cell</th>
<th>Cobalt (II) complex of pyrimidine /cell</th>
<th>Cobalt (II) complex of pyrimidine and Colchicines /cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>The cell which no divided</td>
<td>12%</td>
<td>52%</td>
<td>57%</td>
</tr>
<tr>
<td>The cell which divided</td>
<td>88%</td>
<td>48%</td>
<td>43%</td>
</tr>
</tbody>
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Table 1: Effect of Colchicines and Cobalt (II) complex of pyrimidine inchromosomal cells
Fig. 1: Chromosomal division by use the cobalt (II) complex of pyrimidine derivative

Fig. 2: Chromosomal division by use the Colchicines

Fig. 3: Chromosomal division by use the Colchicines & cobalt (II) complex of pyrimidine
REFERENCES
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