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RESEARCH ARTICLE
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AN INSTANCE GROWING OF BLOOD-PLASMA PROTEIN AND LIVER FUNCTION, BY CHEMOTHERAPEUTIC DOSE OF ANTICANCER DRUG ABRAXANE AND FAMARA IN BREAST CANCER PATIENTS OF HUMAN FEMALE.

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ABSTRACT

In all over the world, the present harmful life threatening situation to face women despite using several effective drugs to reduced the possibility of spreading breast cancer become dominant. The chemotherapeutic chemicals are limited to human (HER2) epidermal growth factor receptor-2. For the purpose of different drugs used against the breast cancer treatment, to evaluate their effects to collect the data of 200 breast cancer women from DHQ Hospital DERA GHAZI KHAN. Our current aims to analysis the blood chemistry of the breast cancer patients and liver functioning test first 5 days and 45 days of the drug use. All the 200 patients are used two different anti-cancer drugs Famara® and Abraxane®. Famara® (Letrozole) is a type of hormone therapy drug and dose of letrozole is one 2.5mg tablet administered once a day without being regards the meals. Abraxane®, the current gold standard for paclitaxel (PTX) delivery, has superiority based effects on breast cancer in nanoparticle albumin-bound technology and their dose 260 mg/m2 IV over 30 minutes every 3 weeks. Despite like these advances, further more novel therapy is urgently needed for the improvement of anti-tumor efficacy for breast cancer. In our study, to analyze that the recombinant of two above clinical drugs of Famara® and Abraxane®. Letrozole acts as inhibitor in the female to suppressing the secretion female secondary hormone like estrogen, estrogen hormone involve in the proliferation of breast cancer cells, letrozole reduce the estrogen hormone secretion in female body during the puberty and the possibility of breast cancer is also reduced. Abraxane® migrates to the tumor region by the mechanism of human serum albumin(HSA) and recognize the HE2(+) breast cancer cells to synthesis of EDC/NHS which promote the tubulin dimers assemble to microtubule and tubulin dimers stabilizes microtubules by preventing depolymerization. This study revealed that the Abraxane® are better functionality than Famara® because breast cancer cure rate are higher than Famara® and have less side effects.

INTRODUCTION

Breast cancer can occur when the breast cells mutated by mutation factor and become cancerous cells and multiply without any control and form tumors. Breast cancer can affects female assigned female at birth (AFBA) age older and 50. But breast cancer can also affect male at assigned male at birth (AMAB). Many treatments to kill the cancer cells and surgery to remove the cancer cells provide by healthcare. Breast cancer is the type of cancer that forms in the cells of beast. Breast cancer occurs both male and

female but more common in female. The trans-membrane signal produced by glycoprotein receptor tyrosine kinase which are stimulated by a chemical messenger receptor2 site are human epidermal growth factor (HER2) leading to cell growth and differentiation[1].

In humans erB2 tyrosine kinase receptor also known as Her2 and is the member of epidermal growth factor receptor (EGFR) family which also include Her3 and H er4.In first time erBs were discovered in an avian erythroblastosis which exhibited similarities to human epidermal growth factor receptor like tumor virus [2].

The HER2 is three epidermal growth factor thought to be an orphan receptor lacking a ligand and forms heterodimers with any of the related receptors, resulting in receptor site activated [3]. The affibody that attached with HER2-binding site are strong binder molecule and thermodynamically stable in structure. But these affibody molecules are interconversion on the sub-millisecond in free state and also shows a clear correlation between the site of dynamics and mutation.The tyrosine kinase receptor phosphorylation site serve as a scaffold for adaptor molecules, enzyme facilitate to down-stream signaling, closely related to Janus kinases and in the same family is a C- terminal tails [4].

Liver toxicity is produced through different pathway by the use of chemotherapeutic agents in different categories of liver injuries but these drugs are not same hepatotoxic. Mostly the anticancer drugs like Abraxane used to induce hepatotoxic and influenced by multiple factors [5].

The Her2 are type 1 trans-membrane protein and with a ligand binding site in extra-cellular sections that containing four domains respectively (I, II, III, and IV), a single trans-membrane helix and kinases most closely related to the Janus kinase [6].

In human HER family of epidermal growth factor receptors consists of four members like HER1, HER2, HER3 and HER4. The receptors for the HER have important roles in the network of stimulating cells signal and controlling cell differentiation and growth. The HER2 receptors are strictly controlled in normal cell. [7]. In human aggressive metastatic disease and breast cancer 20-30% HER2 gene is amplified [8].

Paclitaxel is the strong chemotherapeutic agent which proves the against the breast cancer. For the proper action of paclitaxel need the solvent like lipid based polyoxyl castor oil as a vehicle which can cause histamine-mediated hypersensitivity reaction. To despite the use of antihistamine agents and corticosteroid even fatal reactions occur. Cremophor containing preparation of paclitaxel to be infused through non-di phthalate-containing infusion set with inline over 1 to 3 hour depend on dose. Cremophor preclinical data suggest that it alter the phamacdynamics and drug availability of paclitaxel [9].

Recently we have a reported, significant correlation between expression of stem cell and HER2 over expression marker ALDH1 in a series of 491 breast cancer patients [10].

Primary mediators of these signals and also determined whether the cell differentiate, grows, migrates or dies are receptor tyrosine kinases (RTKs). Receptor tyrosine kinases are cell surface allosteric enzymes consisting of single trans-membrane domain that separates an extracellular ligand binding domain from intracellular kinase domine.Receptor tyrosine kinase are activated by ligand binding induces receptor homo-or heterodimerization and subsequent recruitment of target protein, that activate a complex signaling cascade that leads into distinct transcriptional program [11].

HER ligands can be divided into three groups, the first one is that includes EFG, ampiegulin (AR), transforming growth factor-a (TGF-a) which bind specifically to HER-1. The 2nd group includes betacellulin(BTC), heparin-binding(HB) and epiregulin(EPR) [12] which show the specificity for HER-1 and HER-4

Receptor tyrosine kinases (RTKs) is the receptor for HER family, HER consist of four receptors; epidermal growth factor receptor (EGFR) also known HER-1 or erbB-1, HER-2 also known erbB-2 or Neu, HER-3 are known as erbB-3 and HER-4 are called erbB-4. Approximately nine different homodimers and heterodimers of HER protein exist, but their biological origin displays a distinct hierarchy. HER-2 plays a significant role in each receptor with a specific ligand appears to prefer, HER-2 as its heterodimeric partner [13].

HER-2 is an essential role for mid-gestation development and embryonic lethality [14]. HER-2 also role in production the development of Schwann cell lineage and also analyzed mutagenesis conditions [15]. In the Creallele study, he state that HER-2 mutation occurring in maturing mylinating Schwann cells that

allow the initial development of Schwann cell. HER-2 mutants displayed peripheral nerve hypo-myelination associated with neuropathy and apheno type indulge of the pathology in patients with Charcot-Marie-tooth disease [16].
Over expression of HER-2 associated to shorter time to get well and lower overall survival [17]. HER-2 exert the oncogenic action by the activation of the P1-3K pathways where the inhibition of apoptosis programs [18].

RECEPTOR ON THE MAMMALIAN CELLS

The epidermal growth factor receptors comprises of the four receptor; EGFR-1/ErbB-1, HER-2/ErbB-2, HER-3/ErbB-3 and HER-4/ErbB-4. This transmembane receptor consists of an extracellular ligand-binding domine that activate the cytoplasmic activity like enzyme action [19]. This arrangement of the structure produced signals that to be transmitted across the plasma membrane induces cellular activity such as proliferation by activating the gene expression. There are a number of ligands including neuregulin, EGF-like molecules and transforming growth factor (TGF)-α; these ligands activate the receptor by binding to the extracellular domain and inducing the formation of receptor heterodimers or homodimers. Tyrosine kinase enzyme residues on one receptor are presumably cross phosphorylated to other member of receptor pair and forming the docking sites for signaling complexes composed by adapter protein and cytoplasmic enzyme.
Many different signals transduction cascades such as the mitogen-activated protein kinase pathway (MAPK), anti-apoptotic kinase Akt, phosphoinositol kinas and several transcriptional regulators are stimulated by the activated effector and adapter protein into the cytoplasm by the dissociation of signaling complexes. At last by the receptor ligands complex EFGR signal is inactivated primarily through endocytosis and the content of the resulting endosomes are then either recycle or degraded to the cell surface (reviewed in Ref. [20].

HOW TO GENERATE SIGNAL IN THE CELL FOR PROLIFICATION

The sequence of events known as "signal generation" is attained in RTK-initiated cascades by highly coordinated cellular action. When ligand-binding receptors are first activated, this causes the autophosphorylation of the receptor, which in turn causes the dynamic phosphorylation and dephosphorylation of several proteins. The dynamic state of protein phosphorylation regulates cellular activity and reaction. Depending on the time and location within the cell, a dynamic protein may affect many responses and interact with other proteins. Additionally, various proteins undergo phosphorylation at different places. The first step in comprehending cellular signaling is to measure the dynamics of regulatory site phosphorylation and the consequences that follow in relation to subsequent cell functions. 332 phosphorylated peptides from 175 proteins were found after the analysis. These included 289 singly phosphorylated peptides (tyrosine), 1 triply phosphorylated peptide (tyrosine/tyrosine/tyrosine), and 42 doubly phosphorylated peptides (tyrosine/tyrosine,18 serine/tyrosine, and 3 theronine/tyrosine). There are 20 phosphorylation sites on EGFR, HER-2, and HER-3. HER-3 has one phosphorylation site, eight phosphorylation sites on HER-2, and nine distinct tyrosine and two serine sites on EGRF. Twenty phosphorylation sites on EGFR, Y1005, and Y1127 on HER-2 are present in EGFR family members. These sites are novel, and phosphopeptides containing EGFR Y1114 and HHE-2 Y1005 have been shown to bind SHC [21]. If a mutation occurs on EGFR Y1114, it has been demonstrated to prevent SOCS recruitment to HER-2 [22]. On the basis of quantitative data downstream of the receptor 36 phosphorylation sites on 15 different proteins in the EGFR cone like conical signaling pathway [23].
Review of the cell adhesion pathway embrace quantitative information on 41 phosphorylation sites deliver along 16 proteins contain 9 tyrosine phosphorylation sites on d-catenin. Although HER2 appears to have no intrinsic ligand-binding capability, it can interact reversibly with ligand-activated EGFR or HER3 to form active heterodimers that perturb and often enhance the downstream signals that govern cell proliferation and migration [24].
To assess the effect of increased HER2 expression levels on the canonical EGF-activated pathway, the phosphorylation level for sites observed in EGF-stimulated 24H cells was divided by the phosphorylation level for the same site and stimulation time in EGF-stimulated parental cells, producing a fold change in

phosphorylation level for a given site and time. A subset ofthe proteins and phosphorylation sites within the canonical EGFR signaling network are shown in Figure 4A. As is evident from this figure, increased HER2 expression affects most phosphorylation sites on selected proteins in the EGFR signaling network, but not all phosphorylation sites on a given protein react equally to this perturbation. For instance, each of the multiple phosphorylation sites on EGFR exhibits different regulation at low or high HER2 expression levels, including increased phosphorylation of Y974 and decreased phosphorylation on Y1045 under HER2 overexpression as compared with basal HER2 expression. Both of these sites appear to regulate receptor internalization and degradation: Y974A or Y974F mutations have been shown to decrease receptor internalization rates [25] and Cbl (E3-ubiquitin ligase) binding to EGFR Y1045 is required for lysosomal sorting and receptor degradation [26]. Decreased phosphorylation at the Y1045 site should lead to decreased ubiquitination of activated EGFR, thereby providing a mechanism for the observed increase in recycling of activated EGFR in the 24H cell line relative to parental 184A1 HMECs [27].

In plants and invertebrates, RNA interference (RNAi) has emerged as a highly effective method for specifically suppressing gene expression [28]. According to this method, the Dicer enzyme processes a long dsRNA precursor into 21–23 nucleotides (nt) of complementary short interfering RNA (siRNA), which then effectively silences the targeted gene by binding to complementary mRNA and inducing mRNA elimination [29] showed that transfection of artificial 21–nt siRNA duplexes into mammalian cells efficiently inhibits endogenous gene expression in a sequence-specific manner. Since then, methods based on synthetic siRNA have been employed to silence a number of genes linked to cancer, including polo-like kinase and bcr/abl [30].

FAMARA (Letrozole)

In which one study analysis the accumulative effects of AEE788 with Ietrozole enhanced the antiproliferative effects of the agents by ZR75.1 in MCF-7 by 20-30% cell lines and 60-70% BT474 cell line [31]. The AEE788 partially bring back insensitiveness to letrozole in the model system Ietrozole resistance should be acquired. The inhibition of both HER2 mediated signaling and Mtor-dependent translation brings back responsiveness to Ietrozole in breast cancer [32]. In which one of the study Ietrozole 2.5mg plus lapatinib 1,500mg reduced the positivity of the breast cancer rather than the HER2 increase the positivity of the breast cancer percentage in mostly older women [33]. The combination of the letrozole and bevacizumab was founded well-tolerated and restored drugs toxicities reported were fatigue, headache, hypertension and joint pain [34]. In one of the study combination of adjuvant therapy and chemotherapy for node-negative, ER+breast cancer receive either 7 years of letrozole, the objective of this study to analysis which one is the best therapy of the Oncotype DX gene profiling.

ABRAXANE (Nab-paclitaxel)

In one of the study, anti-HER2 antibody and Abraxane® as sequentially dual therapeutic agent for the breast cancer. Abraxane® and anti-HER2 antibody were conjugated as a stable liker as one drug. Anti-HER2 NPs could first move the tumor site by the mechanism of HSA. The anti-HER2 antibody recognizes the breast cancer cells for improved PTX delivery [35]. Taxanes (Paclitaxel and docetaxel) are highly active drugs for the treatment of breast cancer. Taxanes require solvent to parenteral administration, and the solvent contribute the main toxicities seen with peripheral neuropathy, hypersensitivity and myelo-suppression [36].

The drugs transport into tumors may be enhanced by albumin receptor and caveolae-mediated across the endothelial lining of the cells, for this purpose the nanoparticle albumin-bound pactilaxel is the solvent free formulation of the pactilaxel delivered as a suspension [37].

MATERIAL AND METHOD

Diagnosing breast cancer

Tests and procedures used to diagnose breast cancer include:

1- Beast Exam
Your doctor will check of your both breast and lymph nodes in armpit.

2- Mammogram
The mammogram is X-ray of the breast to use the screen the breast cancer, if any abnormalities doctor recommended other tests.

3- Breast ultrasound
Ultrasound uses sound waves to locate the cancer and image of breast whether breast cancer may be solid or in fluid filled cyst

4- Removing a sample of the breast cancer cells for testing (biopsy).
A biopsy is only way to diagnose the breast cancer, in this method doctor use a specialized needles device guided by X-ray or another imaging test to extract the core of the tissue. The sample are sent the laboratory to test the cells are cancerous are not and then further procedure maybe used.

5- Breast magnetic resonance imaging (MRI).
MRI is machine uses a magnet and radio waves to take the picture of internal breast part, before MRI you receive an injection of dye.

Staging of the breast cancer.
Tests and procedures used to stage breast cancer may include: 1) Mammogram of the other breast to look for signs of cancer. 2) Blood tests, such as a complete blood count. 3) Bone scan. 4) Breast MRI. 5) Computerized tomography (CT) scans. 6) Positron emission tomography (PET) scan.

Treatment
Different method used for treatment of breast cancer.

Breast cancer surgery.
Treatment of the breast cancer includes:
Removing the breast cancer cells (lumpectomy). During a lumpectomy, excision of the tumor cells or tissues also contain a small margin of surrounding healthy tissue the sample maybe removing smaller tumors, some people with larger tumors may undergo chemotherapy.

Removing of the entire breast (mastectomy). A mastectomy is an operational method in which to remove all of your breast tissue, most of the cases remove all of the breast lobules, ducts, tissues, fatty tissue and some skin including the nipple and areola.

Removing a limited number of lymph nodes. To locate the position of cancer cells it may be spread to lymph nodes or not, if cancer is not found then other nodes not necessary to remove.

Removing the both breasts. Some women with cancer in one breast but some maybe both, if they have a very increased risk of cancer in the other breast.

Experimental design.
Our experiment contains 200 female that are patient of breast cancer and data are collected from the DHQ Hospital DERA GHAZI KHAN.

Blood sample. Blood also collected from the breast cancer patients and test to liver function test and blood born chemicals, then doctor analyze the disease.

Blood test	Liver test
ESR	Bilirubin Total
Heamoglobin(Hb)	Bilirubin Direct
WBC(TCL)	Bilirubin Indirect
RBC	Alkaline Phosphatase
Platelete(PLT)	SGPT(ALT)
PCV(HCT)	SGOT(AST)
MCV	Albumine
MCH	Protein Total
MCHC	Gamma G.T

Radiation therapy. In radio therapy uses high powered beams of electron such as X-rays and protons to kill the cancers cell. Radio therapy is done by using a large machine that aims the electron beams at your body; external beam radio therapy of the whole breast is commonly used after a lumpectomy. Some side effects of radio therapy include fatigue, such as damage to the heart or lungs and a red, sunburn-like rash where the radiation is aimed.

Chemotherapy.
Chemotherapy is the method in which drugs used to destroy the fast-growing cells, such as cancer cells. Drugs are sometimes given the patients before surgery in women with larger breast tumors. Chemotherapy side effects include hair loss, vomiting, nausea, fatigue, infection, premature menopause, blood cell cancer, Infertility, nerve damage, damage to the heart and kidneys.

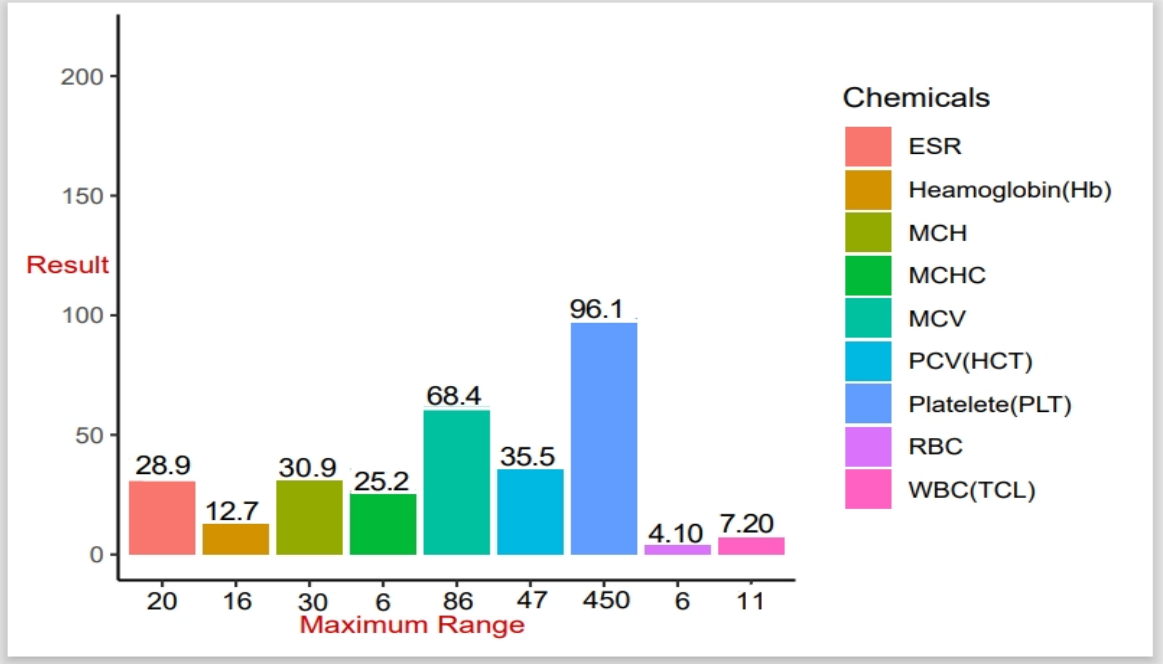
Hormone therapy. A hormone therapy can be used before or after the surgery to decrease the chances of your cancer returning, if the cancer cells spread, hormone therapy may shrink and control it.

Targeted therapy drugs.
Different types of drugs are targeted to the specific types of the cancerous cells in the body. Several drugs are targeted to protein and some breast cancer cells called human epidermal growth factor receptor2 (HER2).First the cancer cells may be tested to see what kind of drugs therapy may be best for cancer cells; others are used in cases of advanced breast cancer to slow the growth of the tumor.

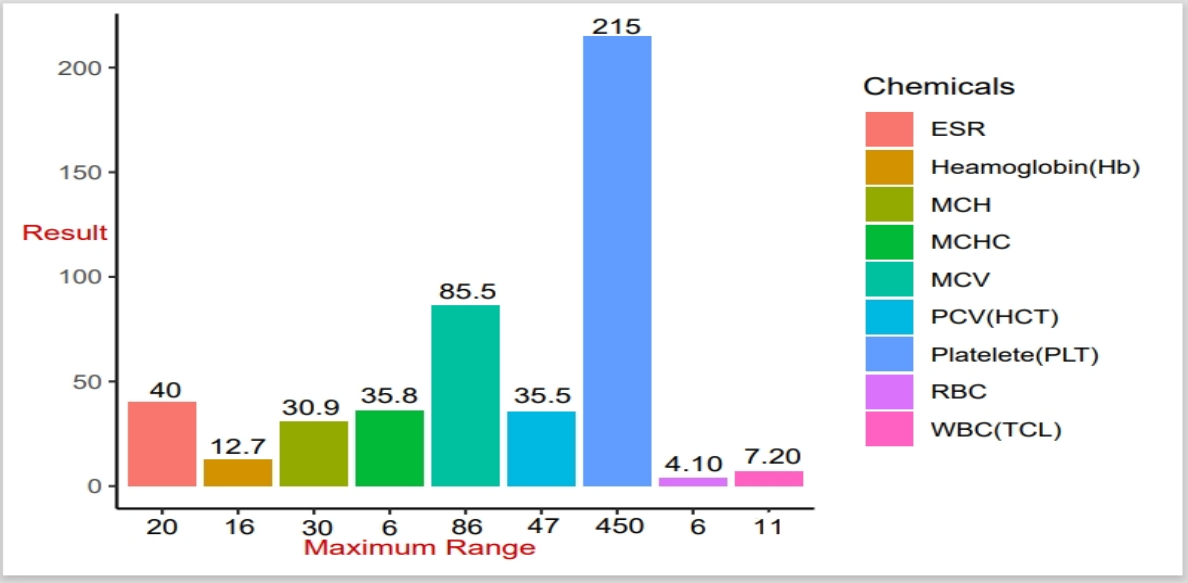
Immunotherapy.
The types of breast cancer treatment in which our immune system immune from the cancer, but some time system will be fail due the cancerous cells produced protein that bind the immune system cells. This method is used if the cancer receptor cells for progesterone, estrogen and HER2.

RESULTS
Our experimental results indicate that Abraxane® and Famara® are greatly influence the hematological parameters amd dysfunction of liver. Different parameters of the blood have increase in valuable range. First five days trial blood sample is taken from 100 breast cancer women the Abraxane drug used patient and value of different parameter are shown in (Graph-1). By using the Abraxane® 45 days, blood sample is collected and measure the different parameters. Significance results, in parameters like platelet (PLT), mean corpuscular volume (MCV), Mean corpuscular hemoglobin concentration (MCHC) and Erythrocyte sedimentation rate (ESR), than fist five days. First five days the parameter counts value, PLT value 96.1.e3/ul, MCV value 68.4fl, MCHC value 25.2G/dl and ESR value 28.9mmlisthour. After the 40 days the parameter counts value, PLT value 215. e3/ul, MCV value 85.5fl, MCHC value35.8G/dl and ESR value 40mmlisthour. The use of Abraxane® in breast cancer patients in 45 days shows the significance results (0.05) in blood parameters (Graph-2). The physical symptoms are also indicating on the female body like swelling in a leg, pain in the chest, difficulty in breathing and behavioral effects.

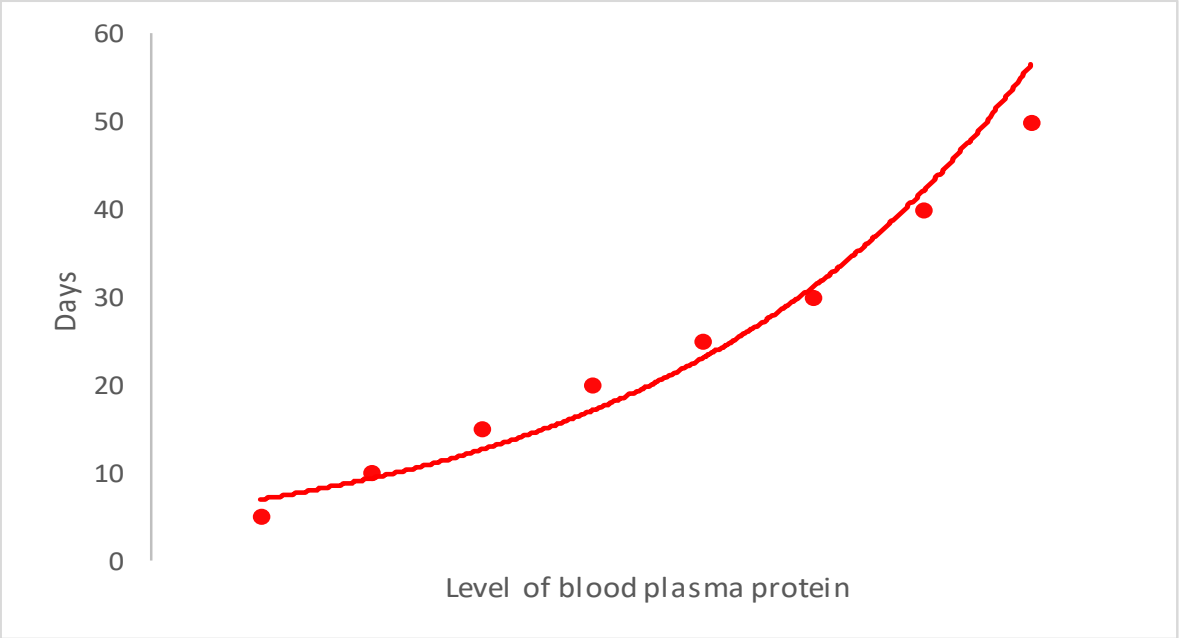
Other symptom is also showing in some patients like loss of appetite, excessive urination, loss of agility and fatigue.



Graph-1-Abraxane used in breast cancer patients and results of blood plasma protein.

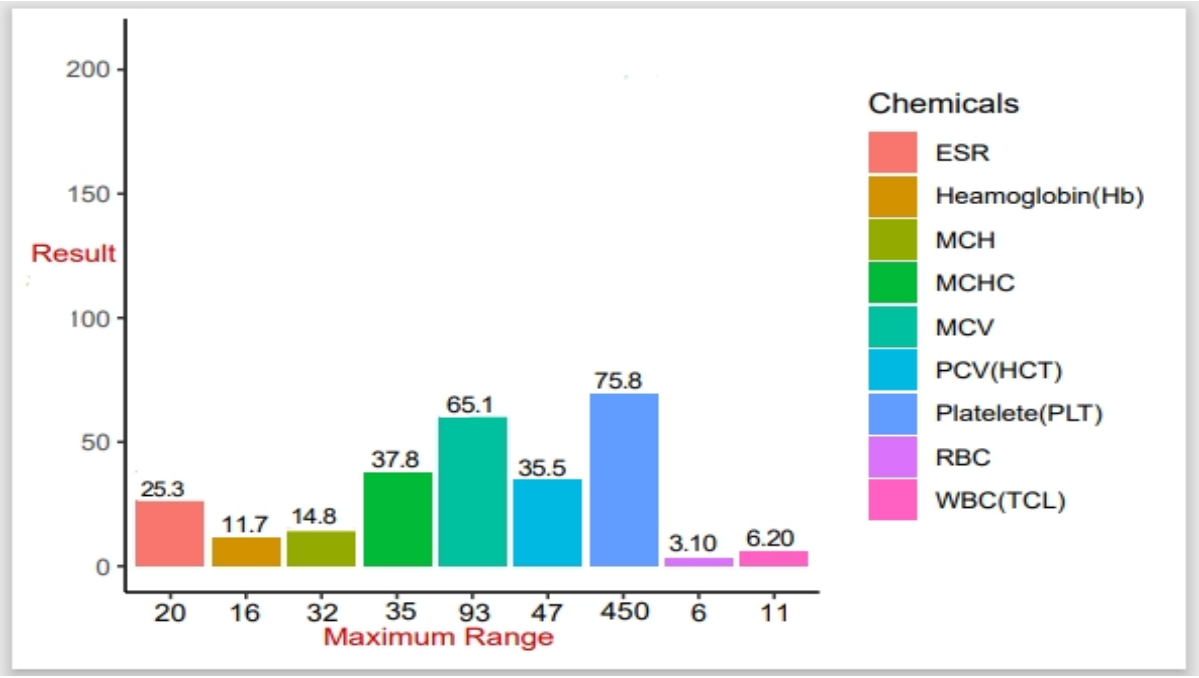


Graph-2-Abraxane used in breast cancer patients and results of blood plasma protein.

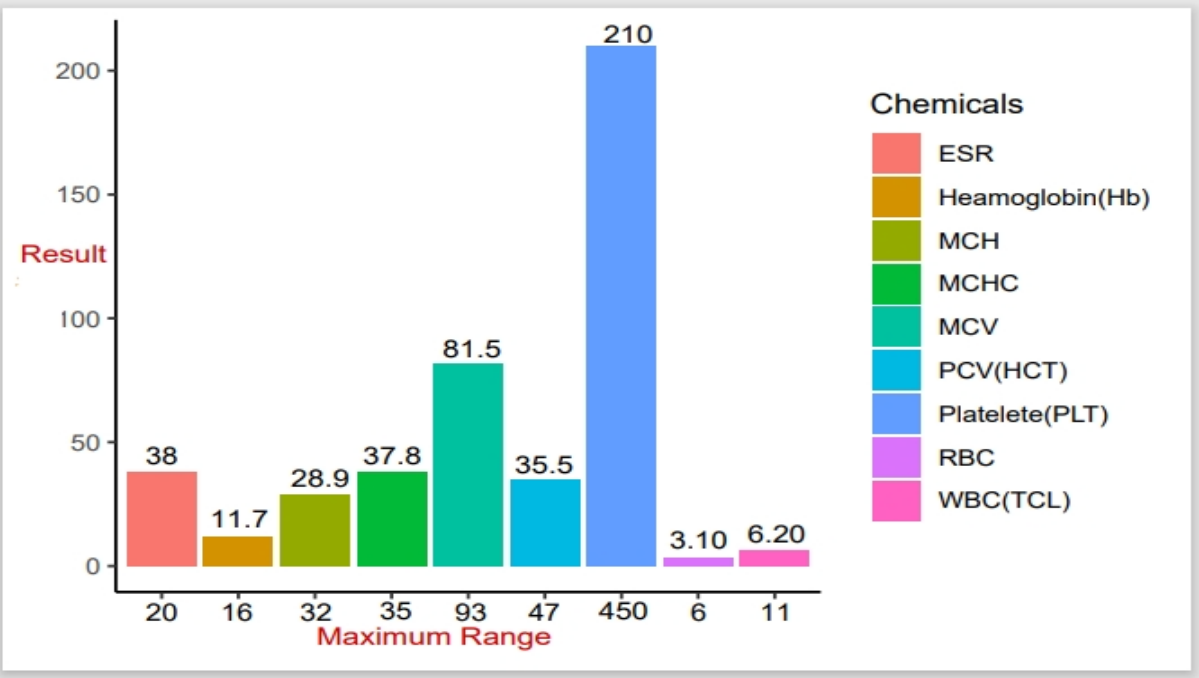


Graph-3 Abraxane effects on blood plasma protein in breast cancer patients.

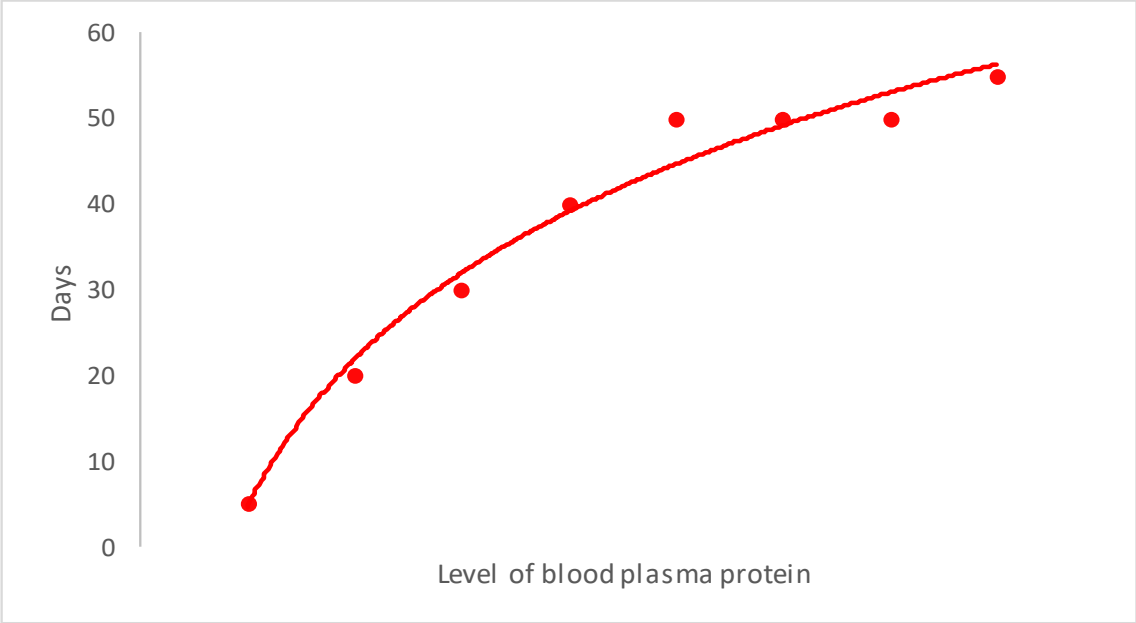
Our investigation is that by use of the Famara® to know their effects on the blood plasma parameters. Different parameters of the blood are influenced by use of the Famara®. First five days trial of experiments to count the blood parameters of all 100 breast cancer women and then 45 days to calculate the value of different parameters. Significance results, parameters like platelet (PLT), mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) and Erythrocyte sedimentation rate (ESR), than fist five days. First five days the parameter counts value, PLT value 75.8.e3/ul, MCV value 65.1pg, MCH value 14.8G/dl and ESR value 25.3.9mmlisthour (Graph-4). After the 45 days the parameter counts value, PLT value 210.e3/ul, MCV value 81.5pgl, MCH value28.9G/dl and ESR value 38mmlisthour. The use of the Famara® in breast cancer patients in 45 days shows the significance results (0.05) in blood parameters (Graph-5). The physical symptom also shows on the human female weight loss, nausea, muscle pain, joint pain, hot flashes, dizziness and double vision in few patients.



Graph-4-Famara used in breast cancer patients and results of blood plasma protein.

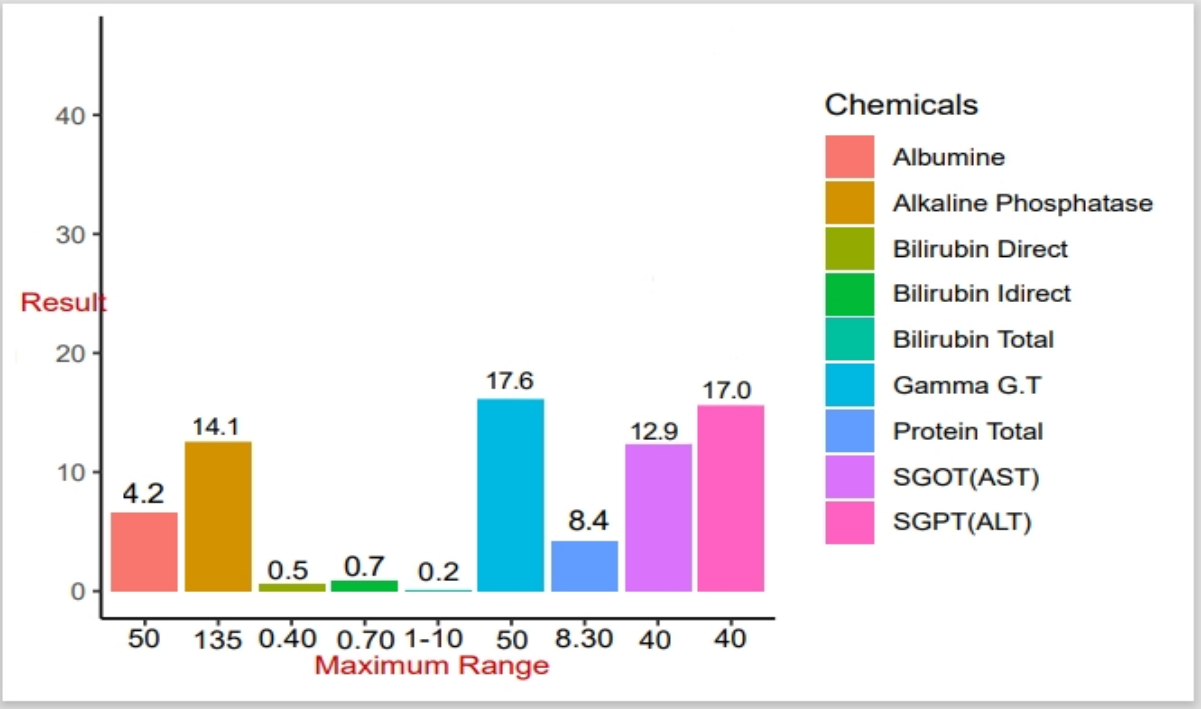


Graph-5-Famara used in breast cancer patients and results of blood plasma protein.

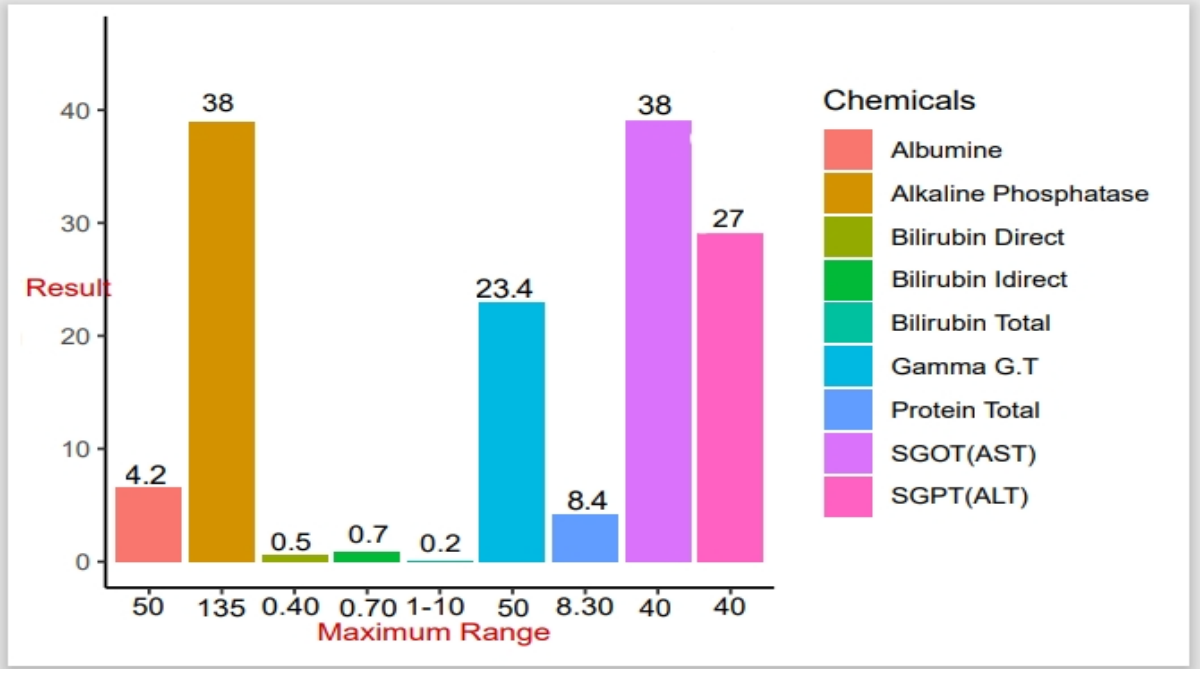


Graph-6 Famara effects on blood plasma protein in breast cancer patients.

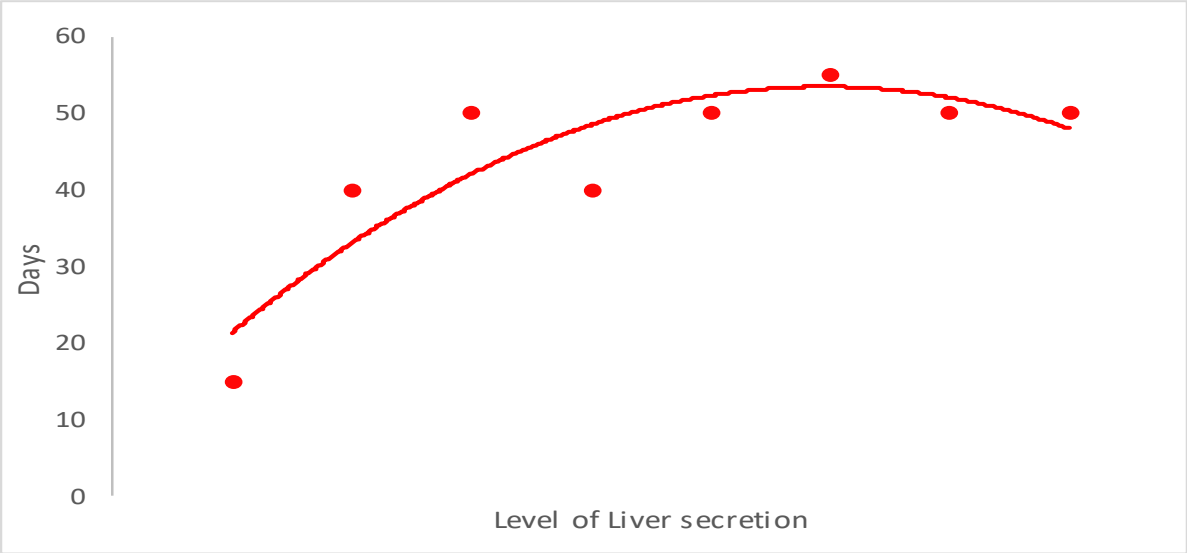
Our experimental results indicate that the drugs Abraxane® and Famara® influence function of the liver. First five days of drugs usage of Abraxane® to calculate the value of concentration of parameters of the liver and after 45 days. The significance results obtain in serum glutamic-pyruvic transaminase SGPT (ALT), serum glutamic-oxaloacetic transaminase SGOT (AST), Gemma G.T and Alkaline Phosphatase. First 5 days value of SGPT (ALT) is 17.4U/L, value of SGOT (AST) is 12.9U/L, value of Gemma G.T is 17.6U/L and Alkaline Phosphatase is14.1U/L (Graph-7). After the 45 days the value should be calculated SGPT-27U/L, SGOT-38U/L, Gemma G.T- 23.4U/L and Alkaline Phosphatase 38U/L. The use of the Abraxane® in breast cancer patients in 45 days shows the significance results (0.05) in liver function (Graph-8).



Graph-7 Abraxane used in breast cancer patients and results of liver function.

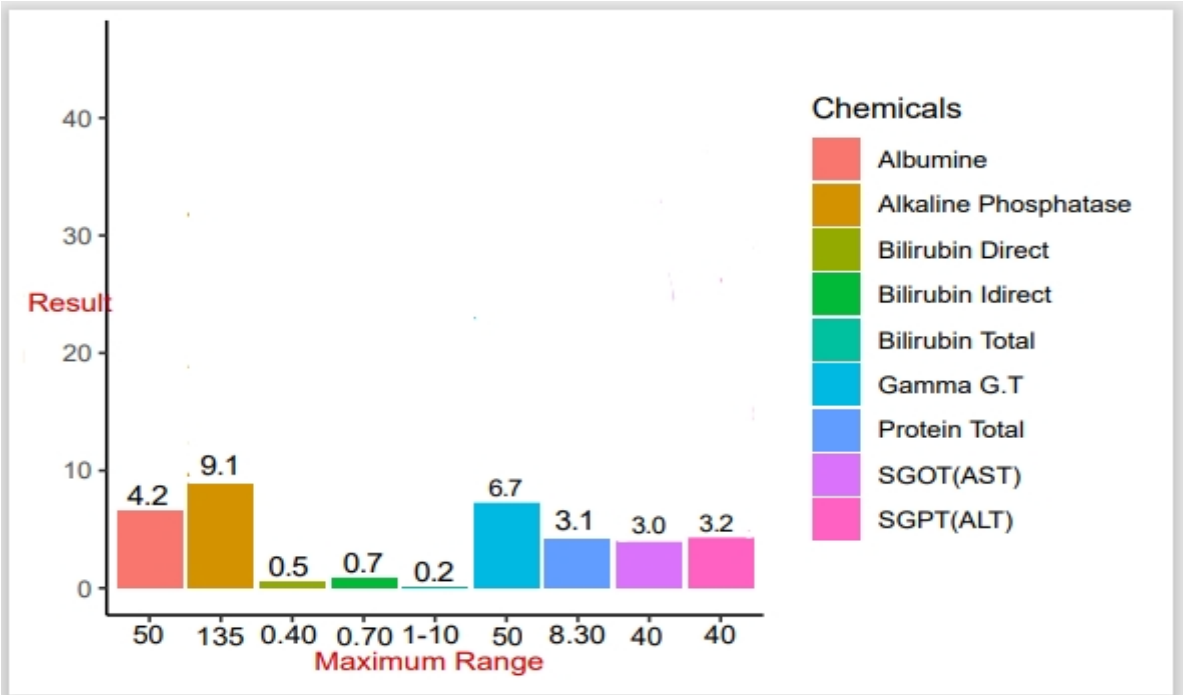


Graph-8 Abraxane used in breast cancer patients and results of liver function.

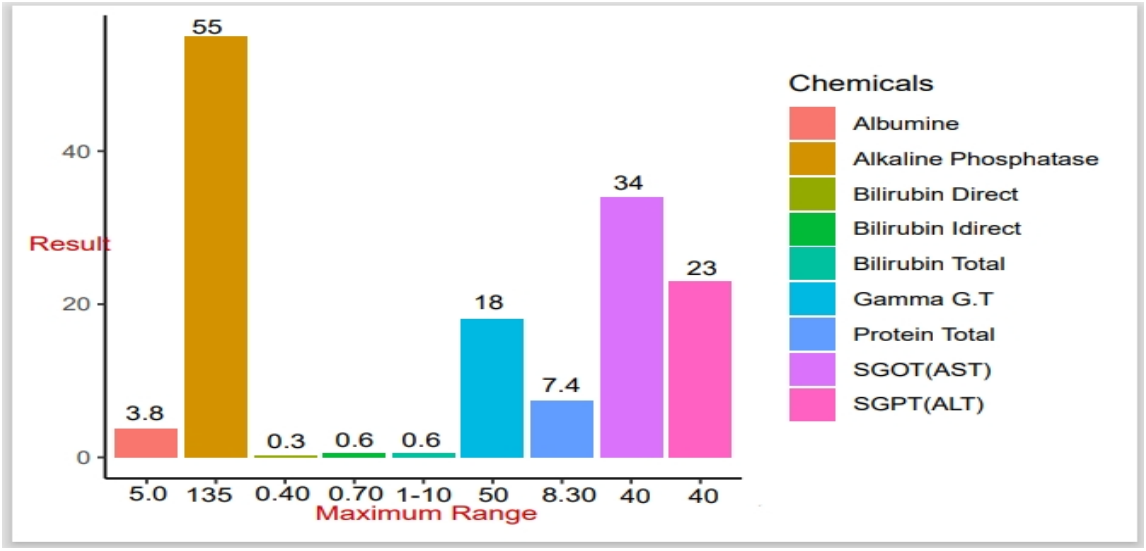


Graph-9 Abraxane effects on the liver function in breast cancer patients

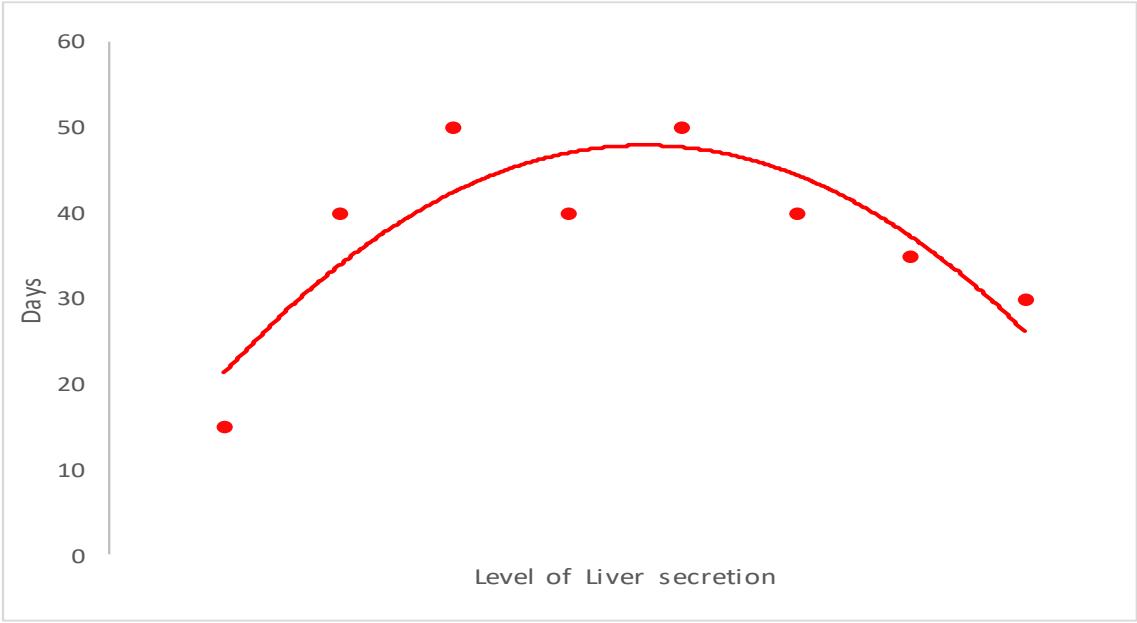
The results evaluate from the experiments Famara® also influence the liver function. The concentration of different parameter of the liver secretion calculated first 5 days and the after 45 days. Significance results obtain in serum glutamic-pyruvic transaminase SGPT (ALT), serum glutamic-oxaloacetic transaminase SGOT (AST), Gemma G.T , Alkaline Phosphatase, Protein total, Bilirubin Total, Bilirubin Direct, Bilirubin Indirect and Albumin. The first 5 days value of SGPT is 3.2U/L, value of SGOT is 3.0U/L, value of Gemma G.Tis 6.7U/L, value of Alkaline Phosphatase is 9.1U/L, value of Protein total is 3.1g/dl, value of Bilirubin Total is 0.2mg/dl, value of Bilirubin Direct is 0.5mg/dl, value of Bilirubin Indirect is 0.7mg/dl and Albumin is 4.2g/dl (Graph-10). After the 45 days value of SGPT is 33U/L, value of SGOT is 34U/L, value of Gemma G.T is 18U/L, value of Alkaline Phosphatase is 55U/L, value of Protein total is 7.4g/dl, value of Bilirubin Total is 0.6mg/dl, value of Bilirubin Direct is 0.3mg/dl, value of Bilirubin Indirect is 0.6mg/dl and Albumin is 3.8g/dl (Graph-11). Famara also reduced the liver function in few patients and decrease the concentration of Bilirubin Direct is 0.5mg/dl value to 0.3mg/dl and Bilirubin Indirect is 0.7mg/dl value to 0.6mg/dl.



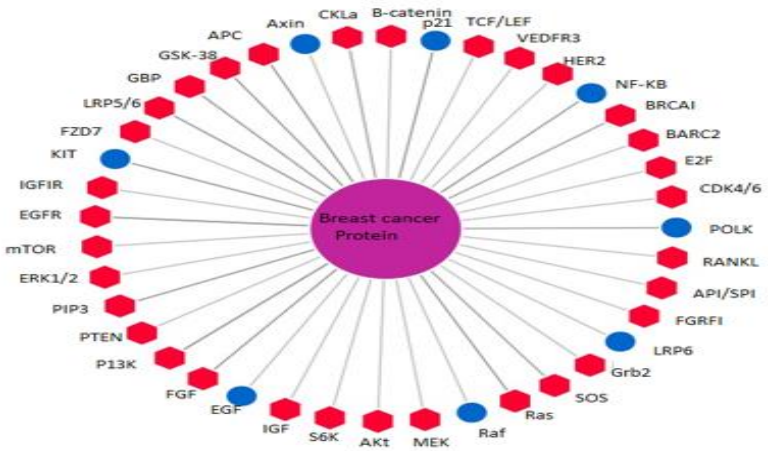
Graph-10 Famara used in breast cancer patients and results of liver function.



Graph-11 Famara used in breast cancer patients and results of liver function.



Graph-12 Famara effects on the liver function in breast cancer patients.



Graph-13 Groups of protein in human female involve in breast cancer growing.

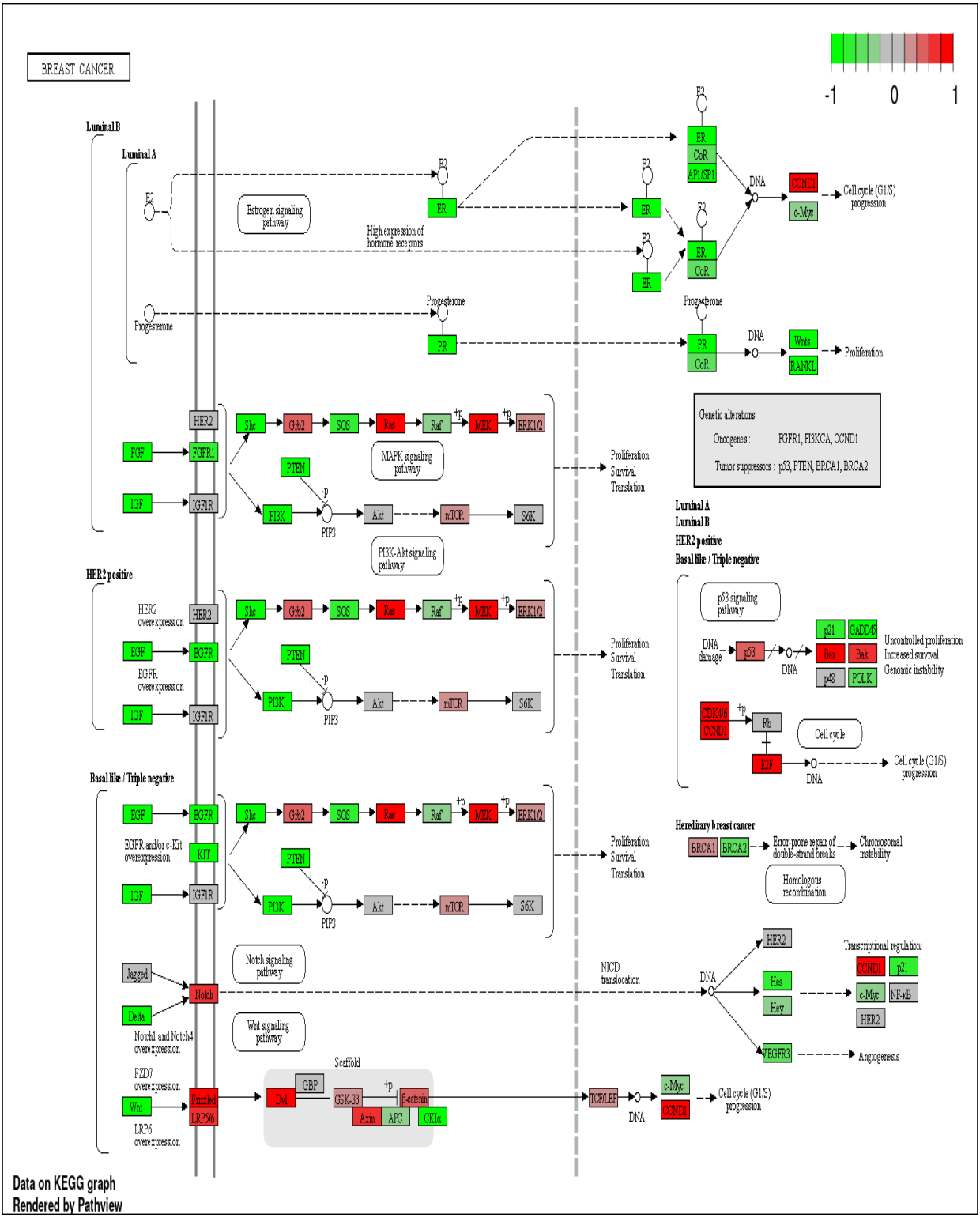


Figure-1 Mechanism of breast cancer in human female.

Discussion

Our experimental results indicate that Abraxane® and Famara® are greatly influence the hematological parameters amd dysfunction of liver. Different parameters of the blood have increase in valuable range. First five days trial blood sample is taken from 100 breast cancer women the Abraxane drug used patient and value of different blood parameters and liver function test are measured show the significance results to increase the concentration of blood plasma protein and liver secretion.

The use of abraxane® most of the patients elevated baseline bilirubin and aminotransferase level. The total bilirubin level were inversely correlated to used of Abraxane® [38]. Physical symptoms are also

indicating on the female body like swelling in a leg, pain in the chest, difficulty in breathing and behavioral effects. Other symptom is also showing in some patients like loss of appetite, excessive urination, loss of agility and fatigue.

By using the Abraxane® 45 days, blood sample is collected and measure the different parameters. Significance results, in parameters like platelet (PLT), mean corpuscular volume (MCV), Mean corpuscular hemoglobin concentration (MCHC) and Erythrocyte sedimentation rate (ESR), than fist five days. First five days the parameter counts value, PLT value 96.1.e3/ul, MCV value 68.4fl, MCHC value 25.2G/dl and ESR value 28.9mmlisthour. After the 40 days the parameter counts value, PLT value 215. e3/ul, MCV value 85.5fl, MCHC value35.8G/dl and ESR value 40mmlisthour. The use of Abraxane® in breast cancer patients in 45 days shows the significance results (0.05) in blood parameters.

In which one of the study indicate that the use of Abraxane® elevated the cholesterol level from 4 to 6% whereas increase the loading was minimal 84 and 85% respectively [39]. By using Famara® Significance results, parameters like platelet (PLT), mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) and Erythrocyte sedimentation rate (ESR), than fist five days. First five days the parameter counts value, PLT value 75.8.e3/ul, MCV value 65.1pg, MCH value 14.8G/dl and ESR value 25.3.9mmlisthour. The physical symptom also shows on the human female weight loss, nausea, muscle pain, joint pain, hot flashes, dizziness and double vision in few patients.

In which one of the study to evaluate that the anticancer drugs used in breast cancer patients reduced the cancerous property in the cells and also dysfunction of many body organ. The used of Famara® anticancer drugs malfunction the hepatic function and blood plasma protein concentration are also disturbed [40].

After the 45 days the parameter counts value, PLT value 210.e3/ul, MCV value 81.5pgl, MCH value28.9G/dl and ESR value 38mmlisthour. The use of the Famara® in breast cancer patients in 45 days shows the significance results (0.05) in blood parameters.

The use of Abraxane® significance results obtains in serum glutamic-pyruvic transaminase SGPT (ALT), serum glutamic-oxaloacetic transaminase SGOT (AST), Gemma G.T and Alkaline Phosphatase. First 5 days value of SGPT (ALT) is 17.4U/L, value of SGOT (AST) is 12.9U/L, value of Gemma G.T is 17.6U/L and Alkaline Phosphatase is14.1U/L.

Liver toxicity is produced through different pathway by the use of chemotherapeutic agents in different categories of liver injuries but these drugs are not same hepatotoxic. Mostly the anticancer drugs like Abraxane used to induced hepatotoxic and influenced by multiple factors [41].

After the 45 days the value should be calculated SGPT-27U/L, SGOT-38U/L, Gemma G.T- 23.4U/L and Alkaline Phosphatase 38U/L. The use of the Abraxane in breast cancer patients in 45 days shows the significance results (0.05) in liver function.

The oxysterol of multiple functions like liver x receptor and tissue specific modulation of estrogen, both receptor seem to adverse effects of 27-hydroxycholestrolsterol in breast cancer and cytochrome p450 CYP27A1 is the only protein that convert the cholesterol into 27-hydroxycholestrolsterol and also increase the level of oxysterol elevated [42].

In gynecological cancer patients chronic kidney disease are more common in such patients anticancer treatment are challenge for clinicians because altered drug pharmacokinetics. The drugs that are excreted mainly kidneys reduced the renal function and increase the toxicity [43].

After the 45 days value of SGPT is 33U/L, value of SGOT is 34U/L, value of Gemma G.T is 18U/L, value of Alkaline Phosphatase is 55U/L, value of Protein total is 7.4g/dl, value of Bilirubin Total is 0.6mg/dl, value of Bilirubin Direct is 0.3mg/dl, value of Bilirubin Indirect is 0.6mg/dl and Albumin is 3.8g/dl. Famara also reduced the liver function in few patients and decrease the concentration of Bilirubin Direct is 0.5mg/dl value to 0.3mg/dl and Bilirubin Indirect is 0.7mg/dl value to 0.6mg/dl.

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