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A REVIEW ON ANTIPROLIFERATIVE ACTIVITY OF PLANT EXTRACTS AGAINST BREAST CANCER CELL LINES

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ABSTRACT: Breast cancer (BC) is the foremost cause of deaths among women worldwide. Plants contain diverse bioactive phytochemicals which have been explored by researchers all over the world for their cancer preventive potential. The present review tabulates *in-vitro* tested plants during 2014-17 against breast cancer cell line. We have collected data of 56 angiosperm families (117 plant species) which was subjected to cluster analysis. On the bases of IC₅₀ values of plant extracts were clustered using cluster analysis Cluster analysis showed a grouping of order Brassicales, Fabales, Lamiales, Caryophyllales, Myrtales, and Apiales. It has been found that most of the plants tested against BC belong to eudicot group of plants. Active plant extract obtained after 24 h, 48 h and 72 h treatment were *Mimosa caesalpinifolia*, *Ferulago angulat*, *Magydaris tomentosa*, and *Ipomea batatas* respectively. These plants may further be characterized for active ingredients to check their prospects in breast cancer treatment.

INTRODUCTION: Breast Cancer (BC) is the most prevalent cause of cancer-related deaths among women worldwide^{1, 2, 3, 4, 5}. Despite advances in its diagnosis and treatment options, the number of incidences is increasing every year^{6, 7}. The number of breast cancer cases reported in 2018 from the whole world was 20,88,849 amongst which 6,26,679 died⁸. BC is not just one disease but has many variations and subtypes with distinct signatures and treatment programs^{9, 10}.

The early stage BC can be successfully cured, but treatment options are scarcely accessible to patients with advanced or metastatic stages⁷. Women with mutated BRCA gene, have nearly 80% risk of developing BC along with a 50% possibility of their children getting the mutated gene¹¹. The genetic mutations in BRCA1 and BRCA2 genes suppurates the exigent root cause of patrimonial breast cancer¹². Although numerous causes are associated with the establishment and progression of BC, yet the oxidative stress (OS) is operating in most of the intracellular pathways concerned with cellular proliferation¹³.

It has been reported repeatedly that the level of OS is higher for BC patients as compared to healthy people due to genetic abnormalities^{1, 14}. This elevated OS is beneficial for malignant cells as it

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upregulates the reactive oxygen species (ROS) mediated signaling pathways which encourage cell growth, cell differentiation, glucose synthesis, protein synthesis and hence cell survival. Numerous ROS are generated within the body as a result of basal metabolic activities. Hydrogen peroxide (H₂O₂) is one such ROS which is generated during estrogen metabolism, and it is known to activate extracellular regulated kinase 1/2 (Erk 1/2). Erk 1/2 is known to promote the survival of breast cancer cells in humans by activating downstream elements¹⁵. Plant extracts being excellent scavengers of free radicals have often been implicated as a remedial measure in various diseases. The plant extracts contain numerous phytochemicals which act synergistically against disorders unlikely the purified compounds¹⁶. Numerous well established anticancer drugs in use today have been derived from plants such as Sulphoraphane, Paclitaxel, Epipodophyllotoxin, Vincristine, Vinblastin, Vinorelbine, Vindesine, Vinflunine, Pomiferin, Roscovitine, Flavopiridol, Noscapine^{17, 18, 19}. In light of the significant contribution of phytochemicals in cancer treatment, the present review was designed to compile the *in-vitro* antiproliferative activity of various plant extracts against breast cancer cell line.

2. MATERIALS AND METHODS:

2.1. Database Search: We have searched online free resource “PubMed” (maintained by National Center for Biotechnology Information at the National Library of Medicine, USA) for plants

extracts assessed for their antiproliferative activity against breast cancer cell line (MCF-7) employing *in-vitro* assays (MTT, MTS, XTT, CCK-8, SRB, CVS, WST-1, ATPlite, Alamar blue, Methylene blue, RTCA MP) for treatment period of 24, 48 and 72 h. The data was collected for the last four years *i.e.*, 2014-17.

2.2. Presentation of Collected Data: The collected data was presented in the tabulated form. Various parameters selected for the present work were a plant, family, plant part used, the solvent used for extraction, assay employed and IC₅₀ concentration.

2.3. Data Analysis: Cluster analysis was done by using PAST software applying Ward’s method, and Euclidian distance was calculated and presented as a measure of similarity.

3. RESULTS AND DISCUSSION:

3.1. Families and Orders: The collected data covered 56 angiosperm families and 118 plants **Table 1**. From these, 50 families belong to eudicots (22 orders), 4 families belong to monocots (4 orders), and 2 families belong to magnoliids (2 orders) as shown in **Table 2**.

3.2. Cluster Analysis (CA): The CA was applied to IC₅₀ values of different plant species (as reported in the respective research paper) on the basis of above-ground plant part with treatment time of 24 (AG24), 48 (AG48) & 72 h (AG72); below ground with treatment period of 24 h (BG24).

TABLE 1: PLANT SPECIES TESTED AGAINST MCF-7 BREAST CANCER CELL LINE DURING 2014-18

S. no.	Family	Plant	Plant part	Solvent	Assay	Treatment time (H)	IC ₅₀ (µg/ml)
1	Acanthaceae	<i>Clinacanthus nutans</i> ³²	Root	MeOH	MTT	24	35
		<i>Avicennia alba</i> ³³	Leaves	MeOH	MTT	48	117
		<i>Ecbolium virde</i> ³³	Leaves	MeOH	MTT	48	60
		<i>Phlogacanthus thyriformis</i> ³⁴	Leaves	EtOH	MTT	24	49
2	Anacardiaceae	<i>Mangifera indica</i> ³⁵	Kernal	EtOH	MTT	72	15
		<i>Lannea coromandelica</i> ³³	Bark	MeOH	MTT	48	270
			Leaves	MeOH	MTT	48	161
3	Apiaceae	<i>Glehnia littoralis</i> ³⁶	Root	AQ	CCK-8	24	158.63
		<i>Ferula heuffelii</i> ³⁷	Underground Parts	CF	MTT	24	6.1
4	Apocynaceae	<i>Leptadenia reticulata</i> ³⁸	Whole plant	AQ	MTT	24	47.6
		<i>Picralima nitida</i> ³⁹	Root Bark	EtOH	MTS	24	740
		<i>Holarrhena floribunda</i> ⁴⁰	Leaves	MeOH	MTT	24	22.76
						48	357.6
						72	244.3
		<i>Hemidesmus indicus</i> ⁴¹	Root	AQ	MTT	24	126.7
						24	829.32

5	Araliaceae	<i>Hedera nepalensis</i> ⁴²	Aerial Part	30% EtOH	MTT	24	209.73
6	Asteraceae	<i>Vernonia cinerea</i> ⁴³	Whole plant	MeOH+ CF	SRB	72	62
		<i>Gnaphalium luteoalbum</i> ³³	Leaves	EtOH	SRB	72	60
		<i>Artemisia indica</i> ³⁴	Leaves	MeOH	MTT	48	340
		<i>Launaea procumbens</i> ⁴⁴	Leaves	95% EtOH	MTT	24	48
		<i>Sphaeranthus amaranthoide</i> ⁴⁵	Whole plant	MeOH	MTT	48	> 80
		<i>Anthemis mirheydari</i> ⁴⁶	Whole plant	PE	MTT	48	23.55
7	Berberidaceae	<i>Berberis orthobotrys</i> ³⁹	Root	DCE	MTT	72	25.2
8	Bignoneaceae	<i>Tabebuia impetigosa</i> ⁴⁷	Dried inner bark	MeOH	MTS	24	81.35
9	Cactaceae	<i>Opuntia ficus-indica</i> ⁴⁸	Stem	MeOH	SRB	24	110.76
10	Caparaceae	<i>Crateva adansonii</i> ⁴⁹	Stem Bark	EA	MTT	48	138
11	Caprifoliaceae	<i>Nardostachys jatamansi</i> ⁵⁰	Roots + Rhizome	DCM + MeOH	ABA	24	289
12	Caryophyllaceae	<i>Arenaria montana</i> ⁵¹	Aerial part	MeOH	MTT	48	58.01
13	Chrysobalanaceae	<i>Licania rigida</i> ⁵²	Seeds	PE	MTT	48	60.59
		<i>Licania tomentosa</i> ⁵²	Seeds	AQ	SRB	48	130.05
14	Combretaceae	<i>Anogeissus latifolia</i> ⁵³	Stem & Leaves	EtOH	ATPlite	24	N.C
		<i>Terminalia bellerica</i> ⁵³	Stem & Bark	EtOH	ATPlite	24	N.C
		<i>Terminalia bellerica</i> ⁵⁴	Fruits	95% EtOH	MTT	48	20.1
		<i>Terminalia chebula</i> ⁵⁵	Leaf galls	95% EtOH	MTT	48	9
15	Convolvulaceae	<i>Ipomoea batatas</i> ⁵⁶	Peeled tubers	70% MeOH	WST-1	48	104.65
			Not Peeled tubers	EtOH	MTT	72	208.16
16	Cucurbitaceae	<i>Momordica cochinchinensis</i> ⁵⁷	Aril	Acidified EtOH	MTT	24	4.9
17	Dilleniaceae	<i>Dillenia suffruticosa</i> ⁵⁸	Root	Acidified EtOH	MTT	48	117
		<i>Dillenia suffruticosa</i> ⁵⁹	Root	Hexane+ Acetone + EtOH	MTT	48	20.3
		<i>Dillenia indica</i> ³³	Leaves	DCE	MTT	24	76
18	Dioscoreaceae	<i>Dioscorea villosa</i> ⁶⁰	Root	EA	MTT	48	340
19	Dipterocarpaceae	<i>Dipterocarpus turbinatus</i> ³³	Bark	MeOH	CC	72	27
20	Droseraceae	<i>Drsera burmanni</i> ⁶¹	Whole plant	MeOH	MTT	48	168
21	Ebenaceae	<i>Diospyros peregrina</i> ³³	Leaves	MeOH	WST-1	48	120.94
22	Ericaceae	<i>Vaccinium bracteatum</i> ⁶²	Leaves	MeOH	MTT	48	7
23	Euphorbiaceae	<i>Jatropha curcas</i> ³⁹	Root Bark	Hexane	RTCA	72	206.75
		<i>Jatropha gossypifolia</i> ³⁹	Root Bark	EtOH	MP		
		<i>Croton sphaerogynus</i> ⁶³	Leaves	EtOH	MTS	24	36.55
24	Fabaceae	<i>Eythrina excelsa</i> ⁶⁴	Stem Bark	EtOH	MTS	24	25.55
		<i>Acacia catechu</i> ⁵³	Fruit	EtOH	SRB	48	53.4
		<i>Acacia catechu</i> ⁵⁴	Heartwood	50% EtOH	MTT	48	13.6
		<i>Enterolobium cyclocarpum</i> ⁶⁵	Leaves	70% MtOH	MTT	48	22.8
		<i>Sophora interrupta</i> ⁶⁶	Root	MeOH	MTT	48	11.84
		<i>Caesalpinia pulcherrima</i> ³³	Leaf	EA	MTT	24	250
		<i>Clitoria ternatea</i> ³³	Flower	MeOH	MTT	48	240
		<i>Alhagi graecorum</i> ⁶⁷	Aerial Part	MeOH	MTT	48	114
		<i>Saraca indica</i> ⁶⁸	Bark	MeOH	MTT	48	170
		<i>Pithecellobium dulce</i> ¹⁶	Leaf	85% EtOH	CVA	48	36.4
		<i>Mimosa caesalpinifolia</i> ⁶⁹	Leaves	80% MtOH	MTT	72	73.6
25	Geraniaceae	<i>Pelargonium sidoides</i> ⁷⁰	Root	AQ	MTT	24	400
						48	300
				70% EtOH	MTT	24	5
				AQ +	SRB	72	43

				Alcohol			
26	Hypericaceae	<i>Hypericum adenotrichum</i> ⁷¹	Aerial part	MeOH	MTT	72	10.9
27	Icacinaeae	<i>Pyrenacantha standtii</i> ⁷²	Leaves	EtOH	MTS	24	37.36
28	Lamiaceae	<i>Teucrium polium</i> ⁷³	Leaves	MeOH	MTT	48	35
			Flower	MeOH	MTT	48	20
		<i>Lavandula dentata</i> ⁷⁴	Whole plant	EtOH	MTT	24	39
		<i>Coridothymus capitatus</i> ⁷⁵	Aerial part	EtOH	MTT	24	100
		<i>Lavandula angustifolia</i> ⁷⁶	Aerial part	Hexane	MTS	24	85.68
				EtOH	MTS	24	179.6
		<i>Stachys acerosa</i> ⁷⁷	Aerial part	DCM	MTT	72	160.3
		<i>Stachys benthamiana</i> ⁷⁷	Aerial part	DCM	MTT	72	71.1
				MeOH	MTT	72	162.4
		<i>Stachys byzantina</i> ⁷⁷	Aerial part	DCM	MTT	72	131
		<i>Stachys lavandulifolia</i> ⁷⁷	Aerial part	DCE	MTT	72	81.2
				80% MeOH	MTT	72	151.7
		<i>Stachys persica</i> ⁷⁷	Aerial part	80% MeOH	MTT	72	104.1
		<i>Stachys pilifera</i> ⁷⁷	Aerial part	DCM	MTT	72	40.9
		<i>Stachys pubescens</i> ⁷⁷	Aerial part	DCM	MTT	72	103.3
				MeOH	MTT	72	146.5
		<i>Stachys spectabilis</i> ⁷⁷	Aerial part	DCM	MTT	72	65.2
		<i>Melissa officinalis</i> ⁷⁸	Leaves	AQ	MTT	48	51
		<i>Nepeta cataria</i> ⁷⁹	Aerial part	MeOH	ABA	48	> 500
		<i>Salvia chorassavica</i> ⁸⁰	Root	MeOH	ABA	48	13
29	Lauraceae	<i>Cinnamomum cassia</i> ⁸¹	Bark	Hexane	MTT	24	34
30	Lecythydaceae	<i>Barringtonia racemosa</i> ⁸²	Fruit	MeOH	MTT	48	57.61
31	Loranthaceae	<i>Plicosepalus curviflorus</i> ⁸³	Leaves	MeOH	CVS	48	20.9
				<i>Macrosolen parasiticus</i> ⁸⁴	Stem	MeOH	MTT
				MeOH	SRB	48	51.9
				AQ	MTT	48	59.33
				AQ	SRB	48	94.58
32	Malvaceae	<i>Theobroma cacao</i> ⁸⁵	Leaf	MeOH	MTT	24	41.4
			Bark	MeOH	MTT	24	72
			Root	MeOH	MTT	24	76.4
		<i>Abutilon theophrasti</i> ⁸⁶	Aerial Part	MeOH	MTT	24	505.8
		<i>Ceiba pentandra</i> ⁸⁷	Stem Bark	PE	MTT	48	152.17
							72
		<i>Hibiscus sabdariffa</i> ⁸²	Fruit	MeOH	MTT	48	112.1
33	Melastomataceae	<i>Melastoma malabathricum</i> ⁸⁸	Leaves	MeOH	MBA	72	7.14
			Flower	MeOH	MBA	72	33.63
34	Molluginaceae	<i>Glinus oppositifolius</i> ³³	Whole plant	MeOH	MTT	48	150
35	Moraceae	<i>Ficus cyathistipula</i> ⁸⁹	Leaves	Aqueous	SRB	48	30
				EtOH	SRB	48	18
36	Moringaceae	<i>Moringa oliferna</i> ⁵³	Leaves	50% EtOH	MTT	48	26.4
			<i>Moringa oliferna</i> ⁹⁰	Essential oil	CP	MTT	24
37	Myricaceae	<i>Myrica nagi</i> ³³	Leaves	MeOH	MTT	48	172
38	Myrtaceae	<i>Syzygium aromaticum</i> ⁹¹	Cloves	EtOH	MTT	48	455
			<i>Pimenta dioica</i> ⁹²	Berries	AQ	MTT	72
39	Oleaceae	<i>Fraxinus micrantha</i> ⁹³	Dried Bark	MeOH	MTT	24	18.95
			<i>Jasminum sambac</i> ³³	Leaves	MeOH	MTT	48
40	Papaveraceae	<i>Chelidonium majus</i> ⁹⁴	Whole plant	EtOH	MTT	24	179.35
							48
		<i>Fumaria vaillantii</i> ⁹⁵	Aerial part	80% EtOH	MTT	24	90
						48	20
						72	2
41	Phyllanthaceae	<i>Flueggea leucopyrus</i> ⁹⁶	Aerial part	AQ	SRB	24	27.89
42	Piperaceae	<i>Piper cubeba</i> ⁹⁷	Seeds	MeH	MTT	72	22.31
				DCM	MTT	72	62.2
		<i>Piper nigrum</i> ⁹⁸	Seeds	93% EtOH	MTT	24	27.1
43	Poaceae	<i>Cymbopogon citratus</i> ⁹⁹	Leaves	50% EtOH	MTT	48	68
				90% EtOH	MTT	48	104.6

44	Potenderiaceae	<i>Eichhornia crassipes</i> ¹⁰⁰	Whole Plant	MeOH	SRB	72	1.2
45	Primulaceae	<i>Aegiceras corniculatum</i> ³³	Fruit	MeOH	MTT	48	91
		<i>Maesa macrophylla</i> ³⁴	Leaves	95% EtOH	MTT	24	22.66
46	Punicaceae	<i>Punica granatum</i> ¹⁰¹	Fruit	Fruit Juice	MTT	72	50
47	Resedaceae	<i>Ochradenus arabicus</i> ⁷⁴	Aerial part	95% EtOH	MTT	24	562
48	Rhamnaceae	<i>Ziziphus spina-christi</i> ¹⁰²	Leaves	80% EtOH	MTT	24	230
49	Rubiaceae	<i>Hymenodictyon excelsum</i> ³³	Bark	MeOH	MTT	48	80
			Wood	MeOH	MTT	48	72
		<i>Mussaenda glabrata</i> ³³	Leaves	MeOH	MTT	48	133
		<i>Galium aparine</i> ¹⁰³	Whole plant	MeOH	XTT	72	503
50	Rutaceae	<i>Glycosmis pentaphylla</i> ¹⁰⁴	Leaves	PE	SRB	48	95.5
51	Salicaceae	<i>Casearia sylvestris</i> ¹⁰⁵	Leaves	AQ EtOH	MTT	24	141
52	Solanaceae	<i>Capsicum annum</i> ¹⁰⁶	Seeds	AQ	CPC	120	14.7
53	Thymelaeaceae	<i>Phaleria macrocarpa</i> ¹⁰⁷	Fruit	AQ MeOH	MTT	24	96
			Seed	AQ MeOH	MTT	24	12
54	Urticaceae	<i>Urtica pilulifera</i> ⁷⁵	Aerial part	EtOH	MTT	24	63
55	Verbenaceae	<i>Lantana camara</i> ¹⁰⁸	Whole plant	EtOH	MTT	24	32.39
		<i>Clerodendrum viscosum</i> ³³	Leaves	MeOH	MTT	48	50
56	Zingiberaceae	<i>Curcuma zedoaria</i> ¹⁰⁹	Rhizome	Hexane	MTT	72	18.4
		<i>Etingera elatior</i> ¹¹⁰	Flowers	Water + EtOH	MTT	72	173.1
		<i>Alpinia galanga</i> ¹¹¹	Rhizome	EtOH	MTT	72	170
		<i>Curcuma kwangsiensis</i> ¹¹²	Rhizome	HD	MTT	24	82.3

N.C = Not Cytotoxic; MeOH = Methanol; EtOH = Ethanol; DCM = Dichloromethane; DCE = Dichloroethane; PE = Petroleum ether; EA = Ethyl Acetate; ABA = Alamar Blue Assay; CC = Cell Counting; CVA = Crystal Violet Assay; MBA = Methylene Blue Assay; CPC = Coulter particle counter; AQ = Aqueous; CF = Chloroform; HD = Hydrodistillation; CP = Cold Pressing; CPC = Coulter particle counter; MBA = Methylene blue assay.

TABLE 2: NUMBER OF ORDERS AND FAMILIES OF PLANT SPECIES (TESTED AGAINST BREAST CANCER CELL LINE) BELONGING TO VARIOUS APG CLADES

S. no.	APG Clade	No. of orders	No. of families	No. of plants
1	Eudicots	22	50	108
2	Monocots	04	04	07
3	Magnoliids	02	02	03

3.2.1. CA of AG24: AG24 involved 31 plant species belonging to 23 families. The CA of AG24 revealed a clustering of *Crateva adansonii* (Capparaceae) with *Moringa oliferna* (Moringaceae) both belonging to order Brassicales and *Mimosa caesalpiniiifolia* with *Eythrina excelsa* which belong to family Fabaceae and order Fabales **Fig. 1**. The minimum IC₅₀ value was found in *Momosa caesalpiniiifolia* (5.0 µg/ml) while maximum IC₅₀ in *Leptadenia reticulata* (740 µg/ml).

3.2.2. CA of AG48: AG48 involved 44 plants belonging to 31 families. The CA of AG48 showed clustering of *Clerodendrum viscosum* (Verbenaceae) with *Melissa officinalis* (Lamiaceae), both belonging to order Lamiales. Clustering was also observed in plants of Caryophyllales order i.e, *Opuntia ficus-indica* (Cactaceae) with *Arenaria montana* (Caryophyllaceae) **Fig. 2**. The minimum IC₅₀ value was found in *Ferulago angulata* (5.3 µg/ml) while maximum IC₅₀ in *Syzygium aromaticum* (455 µg/ml).

3.2.3. CA of AG72: The AG72 group had 27 plants which were spread across 16 families. The CA presented aggregation of families belonging to order Lamiales and Myrtales. The plants belonging to order lamiales were *Stachys persica*, *Stachys pubescens* and *Stachys byzantinai*.

Order Myrtales included *Pimenta dioica* and *Punica granatum* **Fig. 3**. The minimum IC₅₀ value was found in *Magydaris tomentosa* (0.94 µg/ml) while maximum IC₅₀ in *Galium aparins* (503 µg/ml).

3.2.4. CA of BG24: The BG24 group included 13 plants belonging to 10 families. The CA showed grouping of *Glehnia littoralis* and *Hemidesmus indicus* belonging to family Apiaceae and order Apiales **Fig. 4**.

The minimum IC₅₀ value was found in *Ipomoea batatas* (5.9 µg/ml) while maximum IC₅₀ in *Sophora interrupta* (250 µg/ml).

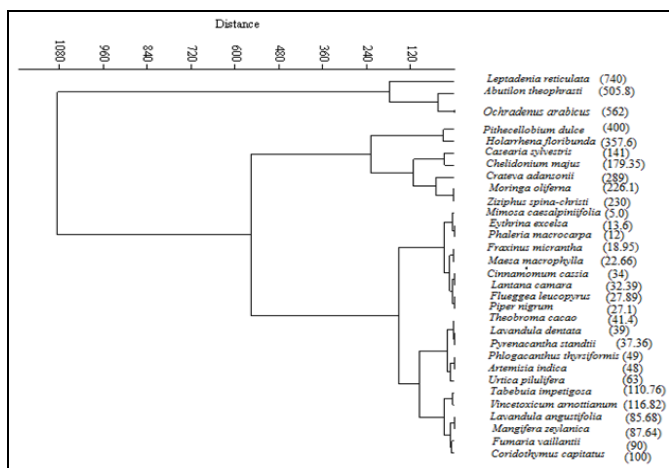


FIG. 1: CLUSTER ANALYSIS OF ABOVE GROUND PLANT PARTS WITH TREATMENT PERIOD OF 24 h (AG24) ALONG WITH THEIR IC₅₀ VALUE (µg/ml)

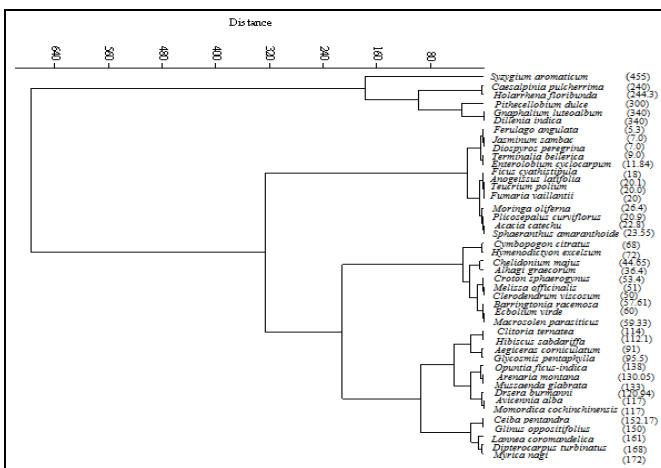


FIG. 2: CLUSTER ANALYSIS OF ABOVE GROUND PLANT PARTS WITH TREATMENT PERIOD OF 48 h (AG48) ALONG WITH THEIR IC₅₀ VALUE (µg/ml)

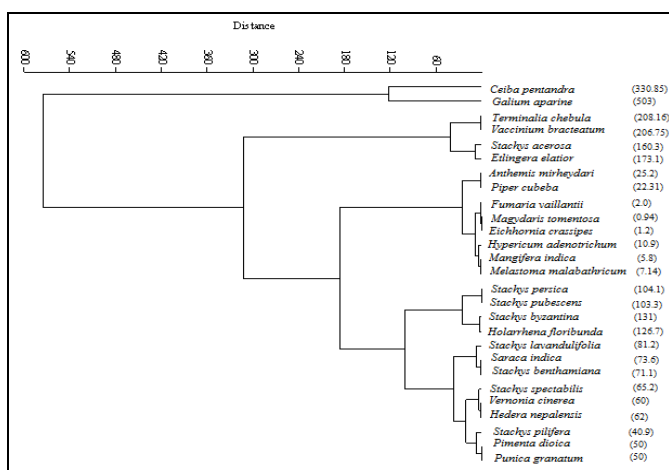


FIG. 3: CLUSTER ANALYSIS OF ABOVE GROUND PLANT PARTS WITH TREATMENT PERIOD OF 72 h (AG72) ALONG WITH THEIR IC₅₀ VALUE (µg/ml)

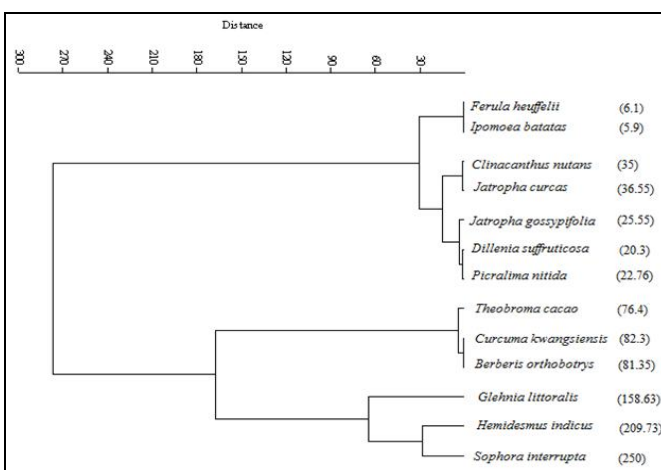


FIG. 4: CLUSTER ANALYSIS OF BELOW GROUND PLANT PARTS WITH TREATMENT PERIOD OF 24 h (BG24) ALONG WITH THEIR IC₅₀ VALUE (µg/ml)

3.3. Assay Reported: The *in-vitro* tetrazolium and resazurin-based reduction assays employed by authors were MTT (3-(4,5-Dimethylthiazol-2-Yl)-2,5-Diphenyltetrazolium Bromide); CCK-8 (Cell counting kit-8); MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt); XTT (2,3-bis(2-methoxy-4-nitro-5-sulphophenyl)-5-carboxanilide-2H-tetrazolium, monosodium salt); SRB (Sulforhodamine B colorimetric assay); ABA (Alamar blue assay); WST (2-(4-iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulphophenyl)-2H-tetrazolium, monosodium salt); Luminogenic ATP (Adenosine triphosphate); RTCA-MP (real-time cell impedance-based cell growth method); CVA (Crystal violet staining).

3.4. Causes of Breast Cancer: There are numerous causes of breast cancers as conversed in proceeding discussion. Elderly women are at more

risk of developing breast cancer as compared to younger women²⁰. Post-menopausal women develop a greater threat of having breast cancer, which doubles with every passing decade to 80 years of life²¹. The risk of getting breast cancer is reduced by bearing a child. This has been justified by the lower rates of incidences in married women as compared to single women²². The reason may be early differentiation of mammary stem cells which belittles the threat of developing breast cancer²³.

Mutations in certain high penetrance genes like RCA1, BRCA2, PTEN, TP53, CDH1, and STK11 and lower penetrance genes (CHEK2, BRIP1, ATM, and PALB2) are responsible for breast cancer incidences^{24, 25}. Long term or frequent exposure to polycyclic aromatic hydrocarbons (PAHs) disrupt estrogen metabolism and induce mammary cancer²⁶.

Most of the ovarian hormones taken after menopause to allay its effects increase the rate of breast cancer induction in postmenopausal women²⁷. Increased alcohol consumption in women is also linked with breast cancer incidences²⁸. Lanky lifestyle like persistent obesity and unhealthy dietary intake is associated with breast cancer²⁹.

Exposure to ionizing radiations especially during breast development elevates the risk of developing breast cancer which can be avoided by lessening repetitive needless testing^{29, 30}. Lopsided work schedule of women in developing as well as developed nations have also been positively correlated to increased breast cancer incidences³¹. **Table 3** and **Fig. 5** compares the number of breast cancer cases reported their percentage of mortality in different countries.

TABLE 3: BREAST CANCER INCIDENCES REPORTED AND PERCENTAGE of CANCER DEATHS IN DIFFERENT COUNTRIES (GLOBOCAN 2014)

Country	Population	Breast cancer	% of breast cancer death cases
India	124×10 ⁷	144937	21.5
Bangladesh	155×10 ⁶	14836	16.9
Afgganistan	29825000	3108	22.8
Australia	23050000	14710	17.3
China	139×10 ⁷	187213	-
France	63937000	54245	19.9
Germany	82800000	71623	18.8
Italy	60885000	50658	18.2
Japan	1.27×10 ⁶	55710	9.2
Pakistan	1.79×10 ⁶	34038	30.8
South Africa	52386000	9815	16
Sri Lanka	21098000	3955	18.8
USA	318×10 ⁶	232714	16.1

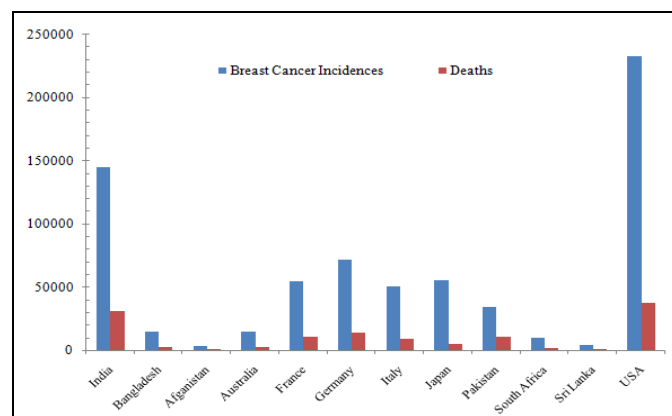


FIG. 5: NUMBER OF BREAST CANCER PATIENTS REPORTED AND PERCENTAGE CAUSALITIES IN DIFFERENT COUNTRIES

CONCLUSION: It has been concluded that most of the plants tested against breast cancer cell line belong to eudicots. Above ground plant parts showed better antiproliferative activity as compared to below ground plant parts. Active plant extract obtained after 24 h, 48 h and 72 h treatment were *Mimosa caesalpinifolia*, *Ferulago angulat*, *Magydaris tomentosa*, and *Ipomea batats*. These plants must be characterized for active ingredients which can further be used *in-vivo* studies in animals induced with breast cancer to find out their prospects in breast cancer treatment.

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