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# EXHAUSTIVE REVIEW ON THERAPEUTICAL ROLE OF SOME PHYTOCONSTITUENTS AND THEIR CHEMICAL ALTERATION

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**Keywords:**

Receptor, Target, Natural chemical template, Semi-synthetic analogues

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**ABSTRACT: Introduction:** Therapeutic agent must be compatible with its target**.** Their multiple interaction produces diversified therapeutic action**.** Chemical exploration of phytoconstituents unravels bio-interaction and strategic engineering of molecules generates wonderful leads in therapeutics**. Method:** The source of information has been accessed through multiple research and review article of peered journals**.** The logical mechanics has been put to churn the spread about phyto therapeutics of natural and its semi-synthetic derivatives**. Result:** For developing and designing a receptor/target compatible structure, chemical diversity of plants provides very good source to have a potent and effective therapeutic agent**.** Study of natural chemical templates helps not only to understand bio-mechanism but also creates a different approach of treatment**.** This review targets different diseases with natural compounds with enlighting the semi-synthetic analogues study of some of them**.** Exploring the chemistry/various character of molecule may provide a better fit model with minimal or no side effect**. Discussion:** On the basis of data processed phytotherapeutics may be explored upfront in pharmaceutical industry**.** These phyto magical entities present the mechanism upto depth of protein, DNA and genetic moulding**.** In future there will be more research ground in this area to produce novel and better alternative for treatment with minimal toxic effects.

**INTRODUCTION:** We generally find many plants treating many diseases**.** So plants are main natural source which provide us different contituents compatible to our body structure. Structure of these plants derived compounds are a better fit model for different receptors.

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As the chemistry of these compounds plays an important role so this review article states about the various plant derived constituents which are used in different diseases and article throw some light on the development of semi-synthetic analogues of phyto-constituents.

The statistical data of each country shows the growth rate in consumption of herbal medicines due to their better desired therapeutic action and less side effects. Market of herbal medicines is raising and getting its place in economy chart. Herbal medicines cover their market in each continent whether Asian market or European. This

raise was not noticed recently in previous decade but before that period**.** Like indicated in the pie chart stats of european market in late nineties [1].

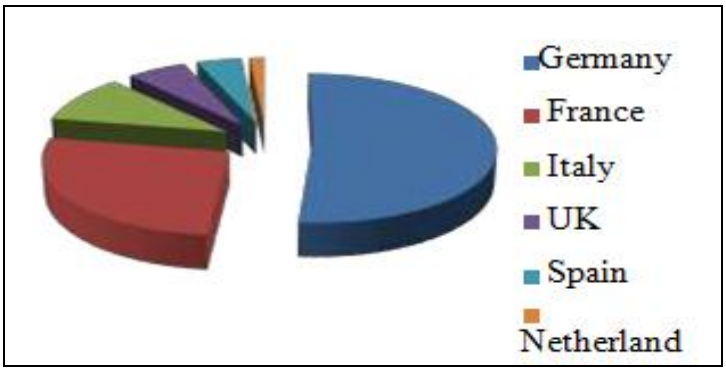


**DIAGRAM 1: EUROPEAN HERBAL MEDICINE MARKET IN 1997 ($ BILLION)**

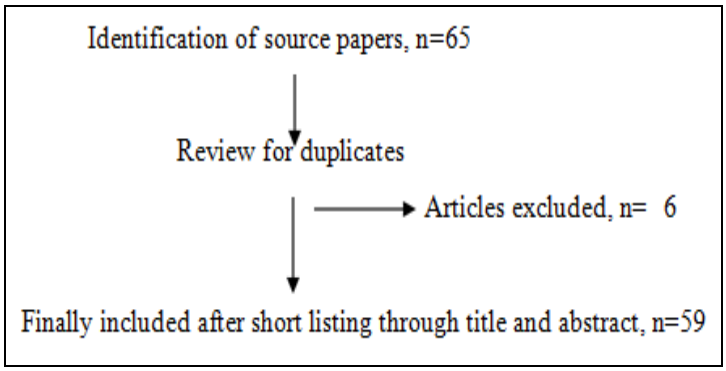


**FIG. 1: DATA ACCESS AND SELECTION**

**Specific Areas with Exhaustive use of Chemical Diversity in Plants:**

**Cardiovascular Disease:** Various chemical nucleus are found in plants which are best suited for the activity in cases of heart disease such as digitalis which having steroidal nucleus**.** Digoxin inhibits sodium-potassium adenosine triphosphatase **(**$Na^+/K^+$ATPase**)** pump resulting into its positive inotropic effect [2]**.** The subsequent rise in intracellular $Ca^{++}$and $Na^+$coupled with the loss of intracellular $K^+$ increases contraction of muscles of heart. Digoxin also increases the automaticity of Purkinje fibers but slows down conduction through the atrioventricular **(**AV**)** node [3]. The phytochemical compounds in tea and coffee with their metabolites modulates gene expression and effect the protective endogenous pathways**.** For the vascular tone is regulated by the effects on endothelial function, increased reverse cholesterol transport and inhibition of oxidative stress and platelet function [4].

**Anti-diabetic:** Diabetes mellitus is a complex disease where the type-2 diabetes **(**noninsulin-dependent**)** is prevalent**.** Although a good extent of research has been done in this area yet there is great demand for developing new anti-diabetic drugs [5, 6]. The side effects of synthetic drugs are the reason for developing new and better pharmaceuticals as alternatives [7]. This turns the face towards natural sources such as the discovery and development of the biguanides [8]. The insulin-like glucose transport stimulatory activity of tannic acid in 3T3-L1 adipocytes was reported where chemically synthesized 1, 2, 3, 4, 6-penta-O-galloyl-β-D-glucopyranose as well as its natural anomer α-PGG possess activity. It was found to affect the glucose transport, by inhibiting the insulin receptor. α-PGG phosphorylate insulin receptor and Akt, which causes activation of PI 3 -kinase and stimulates membrane translocation of GLUT-4 [9].

**Anti-Hypertension:** Phytochemicals explore the attractive target to develop anti-hypertensive drugs**.** There are many compounds which are having powerful anti-hypertensive action such as reserpine [10] which is a purified alkaloid of powerful hypotensive plant *Rauwolfia serpentine* and magnoflorine, aristolochic acid, aristoloside etc**.** found in *Aristolochia manshuriensis***.** The

thiocarbamate and isothiocyanate fractions of *Moringaoleifera* are used for treatment of hypertension [11]. Another plant in this category is *P. harmala* which biosynthesize harmine, harmaline, harmol and harmaloi owing the antihypertensive effects in anesthetized rats [12]. The flavanoid fraction of *Astragalus complanatus* was found to be effective in lowering blood pressurein both renal hypertensive rats and spontaneously hypertensive rats [13, 14].

**Anti-coagulant:** Pulmonary emboli, deep vein thrombosis, strokes and heart attacks are associated with thrombolic disorders which can be treated better with anti-coagulants. *Eichhornia crassipes* (Pontederiaceae) contains flavonoids, alkaloids, terpenoids, steroids, anthraquinones & cardiac glycosides etc [15]. But the polysaccharides found play their role against coagulation through the intrinsic pathway of the coagulation cascade. The other polysaccharide fraction from *Poranavolubilis* contains mainly galactose, galacturonic acid and mannose causes thrombin inhibition that in turn is mediated by heparin cofactor II but not by antithrombin. The carboxyl group in galacturonic acid is significant in performing its anti-coagulant activity as when this group is reduced the activity disappears [16]. The compounds found in aqueous and ethanol extract of *Synclisia scabrida* significantly (P<0.05) prolonged the prothrombin time of normal plasma, suggesting its anticoagulant properties [17].

**Antioxidant Action:** To fight against the injury in kidney due to oxidative stress phytochemicals act as antioxidant. In this process these reduce the lipid peroxidation and enhance the level of endogenous antioxidants [18]. Plants are rich with the chemical library which response to cancer, mutagenesis, allergy and aging effect due to their antioxidant effect [19] such as resveratrol (3,5,4′-trihydroxy-trans-stilbene) in skin of grapes [20]. Phenolic acids (gallic, protocatechuic, caffeic, and rosmarinic acids), phenolic diterpenes (carnosol, rosmanol, and rosmadial), flavonoids (quercetin, and kaempferol), and volatile oils (eugenol, carvacrol and menthol) and some plant pigments (anthocyanin and anthocyanidin) possess same property [21]. But here the antioxidant action is carried out by inhibiting enzymes to suppress free radical generation or chelating the trace elements or scavenging ROS. Some free radical generating enzymes are microsomal monooxygenase, glutathione S-transferase, mitochondrial succinoxidase, and NADH oxidase which are inhibited by flavonoinds. Epicatechin and rutin are strong radical scavengers and inhibitors of lipid peroxidation *in-vitro*. In flavonoid heterocycle the coplanarity of free 3-hdroxyl play an important role for scavenging ability. The potent antioxidant activity of flavan- 3-ols and flavon-3-ols can be accounted for intramolecular hydrogen bonding in the 3', 4'-catechol [22]. For colchicin a study was carried out in parallel with anti-cancer agent 5-Flourouracil in ehrlich ascites carcinoma control mice. The result of study was indicative of antioxidant activity with a significant (P<0.01) decrease in tumor weight and a significant (P<0.01) improvement in biochemical parameters (insulin, alanine transaminase, aspartate transaminase, alkaline phosphatase, reduced glutathione, superoxide dismutase, glutathione peroxidase etc) [23].

**Hepato Protective Action:** The ethanolic extracts of leaves of *Melia azedarach Linn* and *Brassica oleracea L.var.capitata* ( 300 mg/kg/p.o. and 500 mg/kg/p.o.) had shown potent hepatoprotective activity than *Catharanthus Rosea* in simvastatin induced hepatotoxicity in rats [24, 25]. Anthocyanin cyanidin-3-O-β-glucoside (C3G) increases hepatic Gclc expression which decreases hepatic ROS levels and proapoptotic signaling. It enhances phosphorylation of AMP response element binding protein to bind with DNA so that it can increase the Gclc transcription. Result of a study showed anthocyanin C3G was activating GSH synthesis through a novel antioxidant way against excessive ROS production and thus preventing the hyperglycemia-induced hepatic oxidative damage [26]. Silymarin may be of use as an adjuvant in the treatment of alcoholic liver disease [27]. Silibinin, silydianine, and silychristine constitute a flavanoid found in *Silybum marianum*, Compositae [22]. Silymarin causes cell proliferation to regenerate the by increasing biosynthesis of RNA, protein and DNA by stimulating DNA-dependent RNA polymerase 1 enzyme.

It mediates its action through inhibition of leukotriene, ROS scavenging, suppression of NF-κB activity etc [28]. The ethanolic extract of *Mirabilis*

*Jalapa Linn* leaves in dose of 250 mg/kg and 500 mg/kg with anti-tubercular drugs significantly reduced liver biomarker enzymes**.** Different antioxidant parameters were suppressed and increased TBARs levels in anti-tubercular drugs administration [29]**.**

**Anti-inflammatory Action:** Several natural products act as anti-inflammatory agents such as curcumin, parthenolide, 1,8-cineole, pseudopterosins, bromelain [30] and volatile oils obtained from lemon grass **(***Cymbopogoncitratus Stapf***)** [31]**.** *Verbascum mallophorums* contains diverse polysaccharides, iroid glycosides and phenylentanoids**.** Verbascoside down regulate the activity of iNOS which follow the signal to produce nitric oxide using L-arginine as a substrate in response to an increase in superoxide anion activated by NF-kappaB [32]**.** Literature has discussed the role of P2XR in pain and/or inflammation by expression in the central and peripheral terminals and spinal cord**.** These P2R receptors are the therapeutic target for a number of naturalproducts [33]**.** In this discussion another important plant is turmeric (curcuma longa) which contain curcumin, zingiberene, demethoxycurcmin, bisdemethoxycurcumin, curcumenol, eugenol**.** These constituents possess antioxidant, anti-inflammatory, anti-mutagenic and anti-HIV activity [34, 35, 36]**.**

**Anti Microbial:** To fight with problem of resistance to anti-microbial compounds phyto-constituents are being explored [37, 38]**.** A number of heterocyclic nitrogenous compounds **(**alkaloids**)** possess antimicrobial action such as diterpenoid alkaloids **(**Ranunculaceae**)** and glycoalkaloid solamargine from the berries of *Solanum khasianum***.** The highly aromatic planar quaternary alkaloidal structure of berberine and harmane causes intercalation with DNA and are highly active against trypanosomes [39]**.** The hydrophobic cation of berberine **(**isoquinoline alkaloid**)** is an excellent DNA intercalator**.** To show its broad-spectrum range including bacteria, fungi, protozoa and viruses it targets RNA polymerase, gyrase and topoisomerase IV**.** Its accumulation in cells is assisted by membrane potential [40]**.** The redox potential of quinone-hydroquinone pair is of importance like ubiquinone **(**coenzyme Q**)** in mammalian electron transport systems**.** Some enzymes help for this system such as polyphenoloxidase which convert hydroxyl amino acids into quinines for examples tyrosine**.** Quinone brings its effect by forming complex with the protein that is responsible for its antimicrobial effects [39]**.** Other secondary metabolites, such as tannins, terpenoids, alkaloids, and flavonoids are also responsible for the anti-microbial activity [41]**.** In a disk diffusion study against *Streptococcus pyogenes, Staphylococcus aureus, E.coli and P. aeruginosa* the result showed highest antibacterial activity with methanolic extract of *C. longa and C. molmol against S. pyogenes and S. aureus* **(**19 mm**)** respectively while minimum activity was observed with aqueous extract of *P. anisum* against *E. coli* and *P.aueroginosa* **(**7 mm**)** [42]**.** The mature biofilms of *Listeria monocytogenes* on polystyrene plates and stainless-steel coupons matrices were inactivated with different plant-derived antimicrobials**.** The result found showed sub-inhibitory concentrations as given-trans-cinnamaldehyde (TC 0.50, 0.75 mM), carvacrol (CR 0.50, 0.65 mM), thymol (TY 0.33, 0.50 mM), and eugenol (EG 1.8, 2.5 mM), and whereas 5.0 and 10.0 mM (TC, CR), 3.3 and 5.0 mM (TY), 18.5 and 25.0 mM (EG) as the concentration for inactivating mature biofilms [43].

**CNS Action:** Sarsasapogenin, a sapogenin found in *Rhizoma Anemarrhenae* showed its effect on learning ability and memory of aged rats and two neurodegeneration models produced either by single unilateral injection of beta-amyloid 1– 40 **(**Aβ1 –40**)** plus ibotenic acid **(**Ibot A**)** or by bilateral injection of Ibot A alone into nucleus basalismagnocellularis**.** The new approach for regulation of learning and memory was presented and the result of study indicated for the modification of the progression of disease [44]**.**

**Anti-cancer Action:** Several flavonols, flavones, flavanones and the isoflavone are reported to have potent antimutagenic activity [45]**.** The carbonyl group at 4$^{th}$ position of the flavone nucleus is essential for their activity**.** Flavonoids work against cancer through a wide range of mechanism as these may down regulate the mutant p53 protein, arrest the cell cycle or act via**.** tyrosine kinase and expression of Ras proteins or may influence the binding of estrogen on the respective receptors [22]**.** In a study involving human breast cancer cell line

MDA-MB468 quercetin (3,3',4',5,7-pentahydroxyflavone) was found to decrease the activity of mutated p53 protein in a time and dose dependent manner [46]. Paclitaxel (Taxol), a terpenoid, found in endangered Pacific yew- *Taxus brevifolia* ( family Taxacae) has specific and reversible stoichiometric interaction with β-tubulin in the microtubule to inhibit cell division, blocking cell mitosis, stabilizing cytoplasmic microtubules. This not only play anti-cancer role but is also being screened for its activity in other diseases like Alzheimer and coronary heart disease. Another commonly used natural compound is curcunmin which has antioxidant, anti-inflammatory, anti-microbial and anti-cancer activity so finds its use in multiple ways as in case of diabetes, allergies, arthritis and alzheimer's disease [47].

Study conducted on RT4V6 and KU7bladder cancer cells showed that curcumin is assisting in DNA fragmentation and helps in apoptosis [48]. Garlic (*Allium sativum*) is very well known for its antimicrobial, antithrombotic, lipid lowering and anti-cancer activity. But the chemopreventive activity is due to the content of organo sulfur compounds like S-allylcysteine and S-allylmercapto-L-cystein which exhibit radical scavenging activity. In several animal model S – allylcysteine inhibits the growth of chemically induced and transplantable tumors [49].

Astaxanthin a carotenoid, is characterized by its polyene chain with polar entities at both the ends. The chiral centers in C-3 and C-3' has –OH groups that generates two enantiomers (3S, 3'S), (3R, 3'R) and one mesomer (3R, 3'S) where the first one is naturally predominant. Like β-carotene and other xanthophylls, such as lutein, canthaxanthin and zeaxanthin, it has common semi-symmetric layout with two terminal carbon rings flanking an extended double-bond hydrocarbon chain, also referred to as the polyene chain but the presence of hydroxyl and keto moieties on both ends make its structure distinctive from other carotenoids [50]. GCS-100 is a polysaccharide derived from citrus pectin [51]. It induces apoptosis by activating caspase-8 and caspase-3 along with proteolytic cleaving of poly(ADP-ribose) polymerase enzyme and affecting antiapoptotic protein Bcl-2, heat shock protein-27, and nuclear factor-kappaB; and prevent vascular endothelial growth factor-induced migration of multiple myeloma cells [52]. An aromatic phytochemical is found in peanuts (*Arachishypogaea*) which is called resveratrol existing in cis and trans forms. It causes inhibition of cyclooxygenase activity and suppresses TNF-α-induced activation of nuclear transcription factors NF- B etc. to reduce the oxidative stress and lipid peroxidation [53]. The catechins found in green tea like (-)-epicatechin, (-) epigallocatechin, (-)-epicatechingallate and (-)-epigallocatechin-3-gallate possess anticancer action. Where the multi-potency of last one make it a promising multiple-targeted anticancer agent. It causes inhibition of mitogen activated protein kinases, growth factor-related cell signaling, activation of activator protein 1, topoisomerase I, matrix metalloproteinases and other potential targets [55].

Study on Capsaicin (8-methyl-N-vanillyl-6-nonenamide) caused apoptosis in highly metastatic B16-F10 murine melanoma cells. It brings about multiple processes to execute its effects such as nuclear condensation, internucleosomal DNA fragmentation, in situ terminal nick-end labeling of fragmented DNA and release of mitochondrial cytochrome c, activation of caspase-3, and cleavage of poly (ADP-ribose) polymerase in a dose-dependent manner. In the experiment a slight down regulation in Bcl-2 expression was found [56].

**Chemical Modification of Natural Compounds:** Natural products are good template and chemical models for developing newer analogues which are more efficient than the previous one. Such examples are synthetic analogues like meperidine (Demerol), pentazocine (Talwin), and propoxyphene (Darvon) which were developed from the structural template of opiate alkaloid morphine and codeine. Likewise, another example is of aspirin which is the derivative of naturally occurring salicylic acid obtained from willows (Salix spp.) [57]. Thiocolchicoside, a semi-synthetic glycoside of colchicinesis used in the treatment of gout and as muscle relaxant. An astonishing example is the structural modification of radical changes in glycone part of anthracycline antitumor antibiotics which is called annamycin.

2-deoxyglycosidic bond was introduced with a liability for enzymatic and chemical break down. Introduction of an equatorial $NH_2$ group act as a

DNA minor grove anchoring element [58]. The calanolide compounds reported here are the first non-nucleoside analogues having dual activity against HIV-1 and HCMV (human cytomegalovirus). Plant-derived and semi-synthetic calanolide compounds with anti-HIV-1 activity were tested for anti-human cytomegalovirus activity. It was found that there is co-relation between anti- HCMV activity and anti-HIV-1 [59]. The semi synthetic 12-keto derivatives inclinated to possess more anti-HCMV activity than the corresponding 12-OH congeners, which possess more anti-HIV-1 action. It appeared that the double bond between 7th and 8th position in the chromene ring holds its effect for both the activities. If the double bond is reduced, then it will lead to increase in EC 50 values and toxicity [60].

Four protozoan species of the genus Plasmodium (*P. falciparum, P. malariae, P. ovale, and P. vivax*) are responsible for malaria. Plant derived and semi-synthetic drugs quinine, chloroquine, mefloquine and artemisinin are used for treatment of malaria. Likewise, several indole alkaloids, derived from African medicinal plants also possess in-vitro anti-malarial activity such as 6-(3- methyl-but-2-enyl)-1,3-dihydro-indol-2-one, 3-[6-(3-methyl-but-2-enyl) - 1H - indolyl] - 6 - (3 – methyl – but – 2 - enyl)-1H-indole or annonidine F. These were found to be active against the multidrug resistant strain K1 of *P. falciparum* (IC 50 = 21 µgmL-1 for each compound) *in-vitro* testing [61]. A number of natural naphthoquinones (lapachol, β-lapachone and its α-isomer) had shown trypanocidal activities against Trypanosomacruzi parasites which is responsible for Chagas disease. These natural quinones were structurally modified for developing new antichagasic [62].

55P0110 is a semi synthetic analogue of multiflorine which showed its anti-hyperglycaemic role with a low risk for fasting hypoglycaemia in mice. Actually, different semi synthetic analogues were designed. Out of which on study it was found that gliclazide (16 mg/kg) distinctly increased the circulating insulin-per-glucose ratio under basal conditions but 55P0110 (90 mg/kg) lacked such an effect [63]. Another such example is found with the modification of lactone ring. The lactone ring is involved in inhibition of important enzyme by causing conformational changes. The heterocyclic ring replacement is of being noticed. As replacement by furan ring decreases interaction energy by 2.8 kJ/mol, the approximate energetic contribution of lactone hydrogen bond. Pyrrolidone instead of furanone prominently decreases enzyme inhibition. As sulphur is also hydrogen bond acceptor so replacement by it has unmodified interaction energy [64]. More potent semi-synthetic anti-malarial analogs of artemisinin with therapeutically important 1,2,4-trioxane core were synthesized [65]. The first-generation semi-synthetic analogs of artemisinin were prepared to solve the solubility problem. The basic strategy was reduction to its dihydro-derivative (dihydroartemissinin) by sodium borohydride and the lactol was converted to its ether (artemether (a), arteether (b), artelinic acid (c)) and ester (sodium artesunate) (d)) derivatives.

Metabolically more stable 10-phenoxy derivatives were designed which were found to inhibit the P-450 mediated oxidative metabolic formation of dihydroartemissinin. The 10- phenoxy derivatives contains a P-450 resistant aryl group in place of the alkyl group in the first-generation analogs, thus prevents dearylation and its subsequent O-glucuronidation to form the inactive polar conjugate. The pH gradient and the weak base "ion - trapping" effect have generated the aza analogs. The nitrogenous analogs are trapped in the paracite due to protonation by acidic condition of food vacuole [66]. Plant derived betulinic acid which is a pentacyclic lupine type triterpene, has shown selective inhibition of the growth of human melanoma cells (neuroblastoma and cancerous cells of ovary) *in-vitro* as well as *in-vivo*.

The finding of study speaks for the enhancement of differentiation and apoptosis of primary leukemia cells. Its several semi synthetic analogues were synthesized and evaluated. Derivatives with cyanoenone functionality in ring A were found to be highly active whereas betulinic acid was inactive in RAW cell assay. A new analogue is significantly more potent and caused significant induction of the anti- inflammatory, cytoprotective enzyme, heme oxygenase-1, in the liver, while betulinic acid was ineffective at this low dose [67]. Some other derivatives were found to be more potent than betulinic acid for inhibiting inducible NO-synthase, activating phase 2 cytoprotective

enzymes and inducing apoptosis in cancer cells. The cyano group is playing a crucial role as addition of a cyano-enone functionality in the ring of chemical structure which enhances the cytoprotective action but replacement of cyano group with a methoxycarbonyl increases apoptosis process [68].

**Future Scenario of Development of New Drugs from Natural Product Research:** A data of year 1996 revealed a good number of prescriptions. An important area of research and development covers natural compounds. About over 50% of the top 20 drugs were linked to natural product research. A number of plants from the 2,50,000 species are still to be explored. After the research done with natural plants still there are many more areas where the same molecules could also be proved useful like as anticancer, antiviral and anti-fertility drugs. This strategy is like targeting multiple targets with a single stone [69].

**Bilateral Picture of Drug Discovery from Natural Resources:** The natural template-based drug development program is associated with few specific advantages: Reduction of pressure on the resource. Drug development from *Rauwolfia serpentina*, *Digitalis purpurea* etc. are the good example to quote. This approach actually amplifies the therapeutic potential of drug molecule in terms of removing the limitation associated with like podophyllin (obtained from *Podophyllum hexandrum*) suffers with dose-limiting toxicity but its semi-synthetic derivative etoposide is free from this problem to a great extent. Exploring drug from natural resources also suffer from some disadvantages like exploitation of plants for the need of getting the basic template from plants. For instance, anticancer molecules like etoposide, paclitaxel, docetaxel, topotecan and irinotecan are utilising its highly vulnerable plant resources for getting the starting material since a complete synthesis is not possible. On the other hand, it is expected that some 25,000 plant species would cease to exist by the end of this century [70].

**DISCUSSION:** This review present the combine diversified approach which includes the role of phyto-constituents from the level of genetic control and this creates interest of researcher towards exploring and unlocking the chemical treasure of plants. The role of phytoconstiuents have their importance at the level of protein targeting, enzymatic control, DNA targeting, gene expression control etc. The compatibility of these natural pharmacophore has good frequency match in biological chemistry of humans.

This surprising pairing of phytoconstituents with our biomolecules has deep impact to an extent that it can potentially modulate the biochemical processes of body to bring the changes in bio indication from disease to healthy status. This is quite interesting when the mechanism of phyto-molecules is viewed and the structural beauty of these molecules are explored for the generation of radicals, ions, complex and chelate formation through different chemical bond formation and release of chemical bond energy but they help the body's natural mechanism unlike the synthetic drug which involve their typical pathological sense.

Previously there are reviews [71, 72] over herbal structures in context with therapeutics. But this review not only reveals the link between phyto-molecule and their targets but also it presents the wider picture of these phyto-constituents in regard to the structural basis where this includes enantiomeric isolation and semi-synthetic analogue approach. The semi synthetic analogues are the chemically engineered derivative which handles the structural regards towards surpassing pharmacokinetics and pharmacodynamic performance of parent molecule. This is noticeable that development of semi-synthetic approach solves the threat of plants being exhausted.

Phyto-molecules and their semi-synthetic analogues are the magical molecules which leave their synthetic competitor behind in terms of better desired action, long term effect and minimal or no side effects. Even the small functionality is of importance like amino group [57] ketone, double bond chemistry [59] lactone ring, heterocyclic feature of rings modulates the interaction level and brings the enhancement of desired action [64] and hydrophobic nature of aryl group at 10$^{th}$ position in artemisinin [66]. The antioxidant properties of these compounds reduce the toxicity of other drugs also [71]. The chirality in the natural constituents leads the synthesis to the asymmetric synthetic or semi-synthetic research [50]. When synthetic approach gets

blind the phytomolecules unfold the hidden side of prevention and cure of disease**.** So, the traditional knowledge with modern technical approach can lead to finding of newer better and potential therapeutic molecules**.** In the discussion it should not be left behind that the phytoconstituents are not only implemented as direct therapeutic agents but also play safe role towards our health in some other way like in form of cosmetic and several herbal preparation for use as toiletries which utilize herbal extract **(**Diagram 2**)** [73] which serve not only for the purpose of fragrance and appearance but also exhert their role as anti-oxidants, anti-inflammatory, anti-microbials, free radical scavengers, anti-aging and wound healers etc

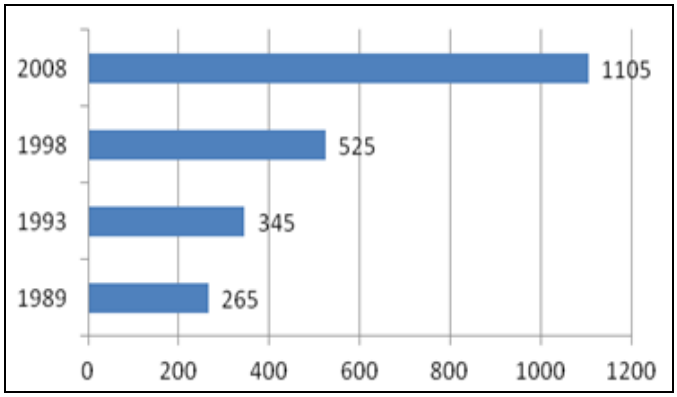


**DIAGRAM 2: BAR CHART SHOWING DEMAND VALUE (BILLION US DOLLAR) OF HERBAL EXTRACT IN COSMETIC AND TOILETRIES IN RESPECTIVE YEARS (Y AXIS)**

**CONCLUSION:** The compounds from the natural sources have the chemistry which is compatible to a number of therapeutic targets in body**.** These are generally having either no or minimal side effects but their comparatively high fruitful therapeutic action make these liable to be explored further**.** On account of avoiding the danger of exploitation, a balanced approach is required in this area so that these can be preserved**.** Semi-synthetic analogue production may be a beneficial because here compounds are modified chemically so that any limitation related to natural compounds may be excluded and the desired properties can be introduced in terms of improved therapeutic potency or modified physicochemical aspects for easy administration to body**.** The utilization and research in this realm may lead to the treatment of those diseases which are till now having no solution or a new better way of treatment may be developed than the existing one**.**

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