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Natural Products And Tradional Medicine In Modern Healthcare

[1]Ms. Priyadarshani Rajkumar Chougule, [2]Ms. Pranjali Prakash Chougule,
[3]Mr. Nikhil RahulChuttar, [4]Mr. Kailash Vanaram Dewasi, [5]Mr. Raghunath Pandurang Raut.
[1]Student, [2]Student, [3]Student, [4]Student, [5]Assistant Professor.
[5]Department of Pharmacology,
Rasiklal M Dhariwal Institute Of Pharmaceutical Education and Research, Acharya Anand Rushiji Marg,Chinchwad, Pune 411019.

Abstract:-
Natural products and traditional medicine have long been integral to healthcare systems worldwide, offering both preventive and therapeutic benefits. This review explores the historical and contemporary roles of natural products, derived from plants, marine organisms, animals, and microorganisms, in modern medicine. Traditional medical systems such as Ayurveda, Traditional Chinese Medicine (TCM), and Indigenous practices have significantly contributed to modern pharmacology, particularly in the discovery of bioactive compounds like alkaloids, flavonoids, terpenes, and polyphenols. Case studies of drugs like paclitaxel, artemisinin, and penicillin illustrate the successful transition of traditional remedies into mainstream medicine.
The paper discusses the biological activities of natural products, including their antioxidant, anti-inflammatory, anticancer, and antimicrobial properties, and highlights their synergy with synthetic drugs. It also examines the integration of traditional and modern medicine in the treatment of chronic diseases and the global efforts, led by organizations like the WHO, to standardize and regulate traditional medicine practices. Despite challenges such as standardization, scientific validation, and ethical concerns, the advancement of technologies like genomics and AI holds promise for the future of natural product discovery and integrative healthcare. This review underscores the importance of collaboration between traditional practitioners and modern healthcare professionals to enhance patient care and global health outcomes.

Keywords:- Natural products, Traditional medicine, Drug discovery, Traditional Chinese Medicine, Ayurveda.

1.Introduction: -

A] Definition of Natural Products: -

Natural products are bioactive compounds or substances that originate from plants, animals, microorganisms, and marine sources. Cohen combines these compounds with secondary metabolites, which as distinct from primary ones that are vital for an organism's existence (for example, carbohydrates or proteins), also have the ecological roles including protection against predators or rivals or information exchange. This sector constitutes the largest source of bioactive molecules employed in traditional systems of medicine and current drug discovery. Due to their different infrastructures and biological functions, they find their applications in many therapeutic classes such as cancer, inflammation, and antibacterial.[1]

I) Plant-Derived Natural Products:-

Among natural products plants have been the most explored source due to use in the earliest form of medicine. They synthesize numerous bio active natural products such as alkaloids, flavonoids and glycosides which has several medicinal uses. For instance, morphine, the alkaloidal compound, is obtained from opium poppy (Papaver somniferum) used a strong analgesic, whereas paclitaxel, the diterpenoid, extracted from the bark of

the Pacific yew tree (Taxus brevifolia) is a standard chemotherapeutic agent today. [2] Approximately a quarter of the prescription medicines to date owe their origin to compounds obtained from plants.

II) Animal-Derived Natural Products:-

Some of the animals also contribute to the pool of natural products more so have not been tendered in comparison to plant products. Snake, spider and scorpion venoms and toxins of other animals possess great pharmacological potential. For example, the peptide structures of reduced molecular weight, such as captopril, mimicked the natural snake venom Bothrops jararaca to change the philosophy of hypertension management. So, in the like manner exenatide, an agent isolated from saliva of Gila monster (Heloderma suspectum), utilised for regulating type II diabetes mellitus.[3] In these examples one can see the promise toward therapeutic usage of bioactive compounds coming from animals.

III) Microorganism-Derived Natural Products:-

Bacteria and fungi are common producers of natural products and these products have been used as antibiotics, antifungal and immunosuppressive agents. Penicillin extracted from the mould Penicillium notatum was the first antibiotic and changed the course of medicine. Other examples among the drugs obtained from fungi are the immunosuppressive agent cyclosporin produced from Tolypocladium inflatum and the antitumor antibiotic doxorubisin derived from Streptomyces peucetius.[4] It has been observed that microbial natural products are still regarded as major source of antibiotics especially at this time that resistance to antimicrobial agents is increasing world-wide.

IV) Marine-Derived Natural Products:-

The marine environment has therefore come out strongly as a major source of natural products due to its huge biological diversity. Six bioactive compounds from sponges, algae, corals, and marine microorganisms have resulted in formation of new therapeutic products. For instance, trabectedin an anticancer drug originally from the marine organism, the Ecteinascidia turbinata. Further, ziconotide which is compound synthetically obtained from the venom of the cone snail – Conus magus is today used as an effective pain reliever, particularly for chronic pain.[5] Marine environment is still poorly explored as source and reservoir of drugs with potential for discovering of new products, the rate of which has potential for being different from those known earlier.

V) Relevance to Drug Discovery:-

Natural products remain a valuable source of new drugs because of their chemical and biological variety. It is they who offer lead compounds or favourites for the creation of new drugs, many of which have multicomponent structures that are challenging to synthesize. It was estimated that over one third and up to half of drugs approved in the recent decades originated from natural products directly or indirectly.[2] Due to their capacity to bind or modulate the biological targets in the human body, these molecular have the potential to become therapeutics across numerous diseases and disorders including oncology, infectious diseases, and immunology.

B] Overview of Traditional Medicine:-

Traditional medicine is defined as the learned, accumulated global experience for the prevention, diagnosis, and treatment of diseases and for the promotion of health anchored in local ethnopharmaceutical knowledge and practices. These systems have developed over time depending on historical and cultural practices as attested to by research. TM is generally associated with holistic health, proactive approach, and reliance on flora, minerals, and animal tissues and organs. Traditional medicine systems are among which Ayurveda, Traditional Chinese Medicine (TCM), Unani, Indigenous medicine systems, and others having placebo concepts and treatment modalities different from each other.

I) Ayurveda:-

Ayurveda is derived from ancient India, over three thousand years ago and is generally classified as whole-istic system based on three basic physiological principles or components known as “doshas;” the Vata (air and space), Pitta (fire and water), Kapha (water and earth). Any imbalance between these doshas is considered unhealthy and illness is a result of having an unhealthy condition. In Ayurveda, treatments include the use of drugs and beverages, which are herbal remedies, changes in daily diet, Panchakarma, Yoga as well as Meditation. The latest Compendium which includes the Charaka Samhita and Sushruta Samhita is specifically dedicated to issues of diagnosis and treatment protocols that are still followed in the contemporary world.[6]

II) Traditional Chinese Medicine (TCM):-

TCM with roots back to 2600 BAC is grounded on the body's energy known as Qi. In TCM, health is considered as the reciprocal influence of yin and yang, and the five phases (Wood, Fire, Earth, Metal, Water). These are well suited and when reciprocally unstable, health is achieved when these are out of balance, disease occurs. Traditional Chinese Medicines are acupuncture, herbal medicine, Tai Chi, Qigong, and dietary therapy to promote the movement of Qi and keep healthy.[7] Today, TCM has benefited the contemporary pharmacology, including new natural substances such as artemisinin to cure malaria.[8]

III) Unani Medicine:-

The Unani system of medicine was originated in Greece but advanced by Arab and Persian scholars and relies on four temperaments – blood, phlegm, yellow bile and black bile. It comprises diet, herbo mineral and physiotherapy treatment to preserve the harmony of these three humors. Unani system of medicine says that when there is imbalance of 'AqalQ – Tar' it results in disease states, and the cures are aimed at the correction of the imbalance. Ilaj bil Tadbeer or regimen therapy, practices like cupping, leaching and massaging are a part of Unani system of treatment.[9] But Unani is still in use in some of the regions of South Asia and the Middle East, where it has become a part of a state-supported health care systems.

IV) Indigenous Practices:-

Indigenous medicine is anchored on the carings practices, treatments, and spiritual interventions that Indigenous people use all over the world. It is however important to note that these systems are very much connected with the local culture, ecology and religion. Traditional Indigenous chemotherapy entails the utilization of indigenous plants, animals' body parts, minerals and prayers to cure physical, mental as well as Spiritual illnesses. Various medicinal plants known and used by Indigenous people in the Amazon region, Africa, North America have benefitted modem pharmacology. The integration of indigenous knowledge in drug discovery has shown to lead to discovery of many bioactive compounds with medicinal values.[10]

V) Global Relevance and Integration:-

The WHO to proffer estimates that common use of traditional medicine for some aspect of primary healthcare has been in access by over 80 percent of populace globally especially in the developing worlds (WHO, 2019). There is growing incorporation of TMS into formal health systems as part of the national health care delivery systems especially in Asia, Africa and Latin America where the formal bioscientific system and the TMS systems exist side by side. Widespread use of complementary and alternative medicine CAM in the developed countries has also stimulated the scientific investigation of the effectiveness, safety of traditional medicines as well as the mode of action of old medicine.

Although it had gained significance prominence, the area of traditional medicine suffers a lot of drawbacks including lack of standardization, complications as to its regulation and doubts as to its scientific efficacy. While natural products have advantages, it is necessary to control them in order to obtain constant quality and to study possible interactions with nowadays' pharmaceuticals. Recent studies are directed to the integration of conventional medicine with the assistance of modern medicine to address the challenges of traditional and provide synergy that will help to solve all the problems in the health sector.[12]

C] Importance in Modern Healthcare:-

Traditional medicines and natural foods are popular in the present generation as they have impressive roles in current medicine as sources of medication, non-pharmacologic remedies, and prophylactic care. Thus, these systems provide a diverse source of bioactive compounds that can be elaborated into therapeutic products and vice versa, act in conjunction with established health management strategies in a patient-centric design for health.

I) Drug Discovery:-

Natural products have always been important source for new drugs as people realized in early civilizations. It is important to note that a vast majority of today's pharmaceuticals are developed from, or based on natural products. For instance, finding of paclitaxel from the Pacific yew tree for cancer or artemisinin from Artemisia annua for malaria, are good examples of a possibility of natural source for critical diseases.[2] Due to growing antibiotic resistance and an incidence of chronic diseases worldwide, the need for new drugs is becoming exigent. Ethnopharmacology—systematic search for bioactive molecules in traditional remedies to identify drugs—has proved that traditional systems of medicine possess drugs with therapeutic values. This underscores the importance of embracing research into traditional medicine knowledge as the guide to generating new leads to drugs.[1]

II) Holistic Health:-

The systems of medicines like Ayurveda and Traditional Chinese Medicine (TCM) tend to make use of WHOLE-PERSON, as a principal concept of practising and maintaining health. Traditional systems of medicine, on the other hand, work holistically – that is, they go straight to the root causes of abnormal conditions and strive to right these conditions into order. Such an approach is regarded as conforming to the current tendencies toward considering patient's genetic and environmental backgrounds, as well as lifestyle.[12] Since today's medicine tends to emphasize the patient's value more and more, the approaches of traditional medicine can enhance our knowledge on complicated illnesses that we faced today like chronic pain, mental health illness or autoimmune diseases.

III) Preventive Care:-

Traditional medicine believes in provision of preventive care, modification of behaviour, diet and use of natural treatment with special uses for herbs. In Ayurvedic system of medicine, for example, definite measures regarding the diet and activities are recommended with a view to regulate the doshas so that diseases do not occur. Likewise, the biomedical practices like acupuncture, herbal medication and Qigong aim to improve functioning and prevent conditions that could cause disease through boosting the defense mechanisms.[13] Traditional medicine on the other hand is opposite to the conventional medicine that tends to wait for a disease to manifest before it starts treating. New healthcare strategic model is a reflection of growing burden of NCDs especially in developing world which require focus on early intervention and disease prevention.[14]

IV) Complementary and Integrative Medicine:-

The mainstream use of integrative or complementary approach to health care is gradually integrating into most advanced health care systems across the world today whereby traditional and universal cure are applied together to improve the of any patient. For instance, acupuncture can be applied in treatment and management of pain and herbal supplements in management of side effects of chemotherapy in cancer clients. Integrative medicine for the patient is helpful because it expands the choice of healing practices that in some aspects complement traditional practices and can help cope with the existing chronic diseases.

V) Biocultural and Sustainable Healthcare:-

Genomics and life sciences also extend the concept of biocultural richness and sustainability in health care correspondingly with the revival of natural products and traditional medicine. Numerous indigenous treatments originating from the tropical regions can still be sourced from Biodiversity hotspots which have a direct implication to modern medicine, health care delivery and probably the human existence. This theorisation is important in preventing the depletion of these resources and in safeguarding indigenous knowledge systems for use by future generations.[15]

2. Historical Perspective: -

A] Evolution of Traditional Medicine: -

Traditional medicine involves the use of natural products, and this practice has many roots in history which dates back to many centuries. Natural medicine treatment is as old as man and has been widely used in today's advanced medical institutions. These medicinal systems have horned complex herbal exploitations to modern document herbal, evidenced in various civilizations forming the back bone of much of modern day scientific medical knowledge. It, therefore, becomes easier to comprehend and perhaps better appreciate the links between the conventional and the advanced systems of tackling health issues.

Era/Region	Key Features	Notable Contributions
i)Ancient Civilizations	Use of natural products as traditional medicines in Mesopotamia, Egypt, India, and China.	Documentation of medicinal plants (e.g., thyme, mustard) from 2600 BCE (Mesopotamia); Ebers Papyrus detailing treatments (1550 BCE).[16]
ii)Ayurveda and TCM	Ancient Indian medical system (3000 years old); Traditional Chinese Medicine (2500 years old).	Texts like *Charaka Samhita* and *Huangdi Neijing* outline herbal remedies and health principles.[6]
iii)Greek and Roman Influence	Emphasis on natural products in Greek medicine; higher doses compared to earlier systems.	Hippocrates described 300 plant products; Dioscorides' *Flora Medica* listed over 600 plants.[2]
iv)Islamic Golden Age	Advancement of natural products in medicine during the 8th-14th centuries.	Avicenna's *al-Qanun fi al-Tibb* served as a significant pharmacological manual for centuries.[1]
v)Indigenous Practices	Culturally specific systems utilizing local medicinal plants.	Use of echinacea and goldenseal in North America; cinchona for quinine in the Amazon.[10]
vi)Medieval and Renaissance Europe	Preservation of medicinal knowledge by monks; revival of herbal knowledge during the Renaissance.	John Gerard's *Herball* (1597) compiled European medicinal plants and their uses.[17]
vii)Modern Era	Transition from folk medicine to modern pharmacy (late 1800s to early 1900s); extraction of active compounds from plants.	Discovery of morphine from opium; quinine from cinchona bark; over 50% of modern drugs derived from traditional knowledge.[2]
viii)Integration with Modern Medicine	Incorporation of traditional medicine into contemporary healthcare systems, especially in Asia, Africa, and Latin America.	WHO supports integration of traditional practices into national health systems for disease prevention.[18]

Table 01 :- Evolution of traditional medicine.

B] Transition to Modern Medicine: -

Thus, the shift between the folk medicine and the modern system of medicine has directed the growth of contemporary pharmaceutics and clinical practice. Most of the orthodox drugs owe their antecedents to traditional medicine where natural compounds were utilized in healing. The empirical research on these folk medicines has facilitated the extraction of bioactive compounds that are usually altered or replicated as improved prescription medications.

As an example what was made fro example aspirin was synthesized from salicin isolated from the willow bark this remedy had been used by ancient Greek and Native American doctors. Likewise, Quinine, popular in today's medicine in treatment of Malaria, which is part of World Wide Pharmaceuticals, was developed from the tree known as Cinchona which native South Americans Indians have been using for a number of ailments. Morphine an opioid analgesic was isolated from opium poppy, which has been employed for ages in the Middle Eastern traditional medicine especially for relief of pain.[2] However, one has to understand that TCM has brought a lot to the modern pharmacology, the famous artemisinin derived from the plant Artemisia annua has anti-malarial properties. This discovery was receiving the Nobel Prize in Physiology or Medicine in 2015 in view of its great accomplishment towards the treatment of malaria all over the world.[80]

The practice has persisted up to modern clinical practices especially under the complementary and integrative medicine. Herbal supplements, acupuncture and holistic treatments are slowly finding their place in the conventional health care delivery system for their function in the early prevention, chronic diseases and promotion of general health.[19] This continuous integration of the conventional and the innovative systems further underlines the significance of natural products in the development of medicine.

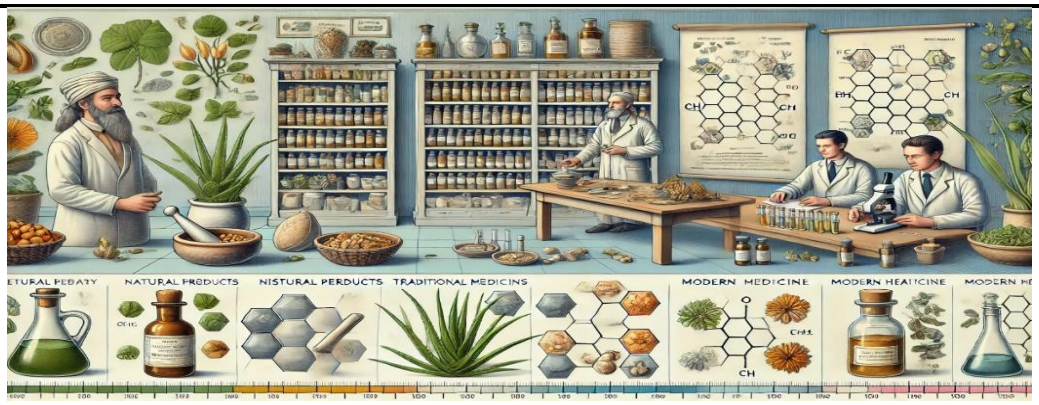

Figure 01 :- Transition of traditional medicine to Modern medicine

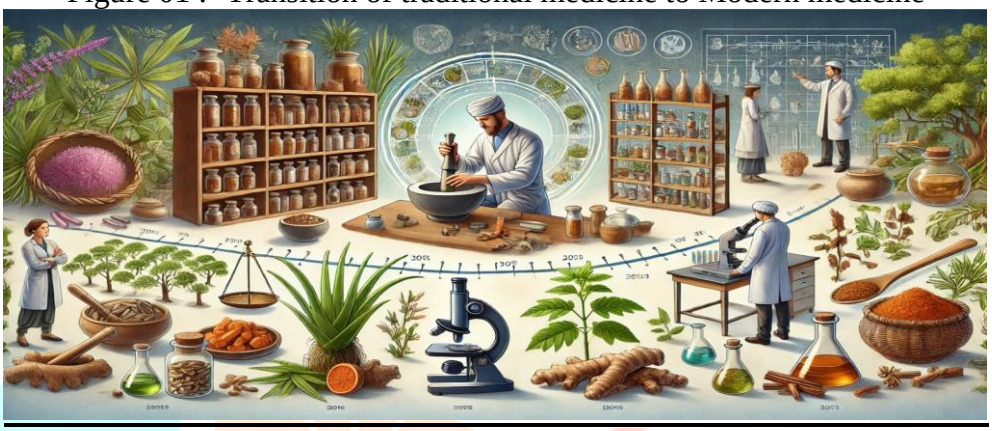

Figure 02 :- Journey of development of medicine from tradition to modern medicine

3. Key Natural Products in Healthcare:-

A] Phytochemicals:-

Plant secondary metabolites known as phytochemicals have been extensively looked at for their medicinally active components. These compounds are of significance in understanding Associations of plant foods and health, as well as a source of lead compounds for drug discovery. The four common phytochemicals that have received much research attention include alkaloids, flavonoids, terpenes and polyphenols that possess diverse pharmacological properties such as antioxidants, anti-inflammatory, anticancer and antimicrobial properties.

Class of Compounds	Description	Key Examples	Biological Activities
i)Alkaloids	Secondary plant metabolites containing nitrogen; widely used in medicine.	**Morphine**: Analgesic from opium poppy (Papaver somniferum).	Analgesic properties; critical in pain management.
		Quinine:Derived from Cinchona tree, historically used for malaria treatment.	Antimalarial activity.
		Vinblastine & Vincristine: Chemotherapy drugs from Madagascar periwinkle (Catharanthus roseus).	Effective against cancers such as Hodgkin's disease and leukemia. Highly active pharmacological actions; models for synthetic drugs.[20]
ii)Flavonoids	Polyphenolic compounds found in fruits, vegetables, and medicinal plants; known for	**Quercetin**: Found in onions, apples, and green tea; anti-inflammatory and anticancer effects.	Scavenges free radicals; reduces oxidative stress and chronic diseases.

	antioxidant properties.		
		Anthocyanins: Responsible for red, blue, and purple colors in berries; powerful antioxidants.	Acts against inflammation and neurodegenerative diseases. Crucial in preventive medicine and nutraceutical development.[21]
iii)Terpenes	Large class of natural products contributing to the aroma of plants; diverse pharmacological properties.	**Taxol(Paclitaxel)**: Diterpene from Pacific yew (Taxus brevifolia); inhibits cell division.	Used in chemotherapy; stabilizes microtubules.
		Menthol: Monoterpene from peppermint; used for analgesic and cooling effects.	Applied in pharmaceuticals for pain relief.
iv)Polyphenols	Compounds with one or more phenol units; primarily found in fruits, vegetables, tea, coffee, and wine.	**Resveratrol**: Found in grapes and red wine; heart protective and anti-aging effects.	Antioxidant properties; potential anti-cancer effects.
		Curcumin:Active polyphenol in turmeric (Curcuma longa); anti-inflammatory and anticancer properties.	Modulates inflammation, oxidative stress, and cancer progression.[23]
		Epigallocatechin gallate (EGCG): Extract from green tea; linked to cancer prevention.	Antioxidant activity promoting cardiovascular and metabolic health. Used in functional foods and supplements for overall health benefits and disease prevention.[24]

Table 02:- Phytochemicals in healthcare

B] Marine Compounds :-

Unique Bioactive Compounds in Modern Drug Development: A large reservoir of marine organisms constitutes bioactive compounds with diversified chemical structures and potent biological activities. The sponges, mollusks, algae, and marine microorganisms constituting such large biodiversity in marine ecosystems have yielded many compounds that have proven significant in modern drug development. Efficacy has been achieved by these marine-derived compounds in regard to cancer, pain, infections, cardiovascular diseases, and other health conditions.

Drug Name	Source	Mechanism of Action	Indications
i)Cytarabine (Ara-C)	Caribbean sponge *Cryptotethya crypta*	Inhibits DNA synthesis in rapidly dividing cancer cells	Acute myeloid leukemia, lymphoma.[25]
ii)Trabectedin (ET-743)	Sea squirt *Ecteinascidia turbinata*	Binds to DNA minor groove, arrests cell division, induces apoptosis	Soft tissue sarcomas, ovarian cancer (especially platinum-resistant cases).[26]
iii)Brentuximab Vedotin	Peptide from *Dolabella auricularia* (sea hare), dolastatin 10	Disrupts microtubule network, leading to cancer cell death	Hodgkin's lymphoma, anaplastic large cell lymphoma.[28]
iv)Plitidepsin (Aplidin)	Marine tunicate *Aplidium albicans*	Targets elongation factor 1-alpha (eEF1A2), affecting protein synthesis in cancer cells	Multiple myeloma, other cancers.[29]
v)Eribulin (Halaven)	Derivative of *halichondrin B*	Inhibits microtubule growth, leading to cell death	Metastatic breast cancer, liposarcoma.[30]
vi)Marine-Derived Antibiotics	Marine sources (*bryozoans, tunicates, bacteria like Salinispora tropica*)	Novel antimicrobial activity, combats antibiotic resistance	Anticancer, antimicrobial activities.[40]

Table 03:- Marine compounds in healthcare

C] Compounds Derived from Microorganisms and Animals in Modern Medicine: -

For many decades, microorganisms and animals have provided the world with a steady supply of bioactive compounds that revolutionize modern medicine. In the case of antibiotics derived from microbes, in particular, antibiotics discovered from microbes have revolutionized the way infections caused by bacteria are treated. The new drugs discoverable from animal venom come up, for example, management of pain, cardiovascular health. Most natural compounds have unique mechanisms of action that are invaluable for drug discovery and development.

Antibiotics Derived from Microorganisms: -

Drug	Source	Mechanism of action	Indications
Penicillin	*Penicillium notatum* (mold)	Inhibits bacterial cell wall synthesis	Pneumonia, syphilis, strep throat, bacterial infections.[31]
Streptomycin	*Streptomyces griseus* (soil bacteria)	Inhibits bacterial protein synthesis	Tuberculosis, bacterial infections.[32]
Tetracyclines	*Streptomyces* species	Inhibits bacterial protein synthesis by binding to the ribosome	Respiratory and skin infections, bacterial infections.[33]
Erythromycin	*Streptomyces* species	Inhibits bacterial RNA synthesis (macrolide antibiotic)	Respiratory and skin infections, bacterial infections.[33]

Vancomycin	*Amycolatopsis orientalis* (bacteria)	Inhibits bacterial cell wall synthesis	MRSA, multi-drug-resistant infections.[34]

Table 04:- Microorganism derived antibiotics in modern healthcare

Compounds Derived from Animal Venoms:-

Drug	Source	Mechanism of Action	Indications
Captopril	Venom of the Brazilian pit viper *Bothrops jararaca*	Inhibits conversion of angiotensin I to angiotensin II, reducing blood pressure	Hypertension, heart failure.[35]
Ziconotide	Venom of the marine cone snail *Conus magus*	Blocks N-type calcium channels, inhibiting pain signal transmission	Chronic pain management (non-opioid analgesic).[36]
Exenatide	Venom peptide of the Gila monster *Heloderma suspectum*	Mimics incretin hormone, promotes insulin release, regulates blood glucose levels	Type 2 diabetes.[37]
Eptifibatide	Venom of the southeastern pygmy rattlesnake *Sistrurus miliarius*	Inhibits platelet aggregation by blocking glycoprotein IIb/IIIa receptor	Prevention of blood clots during heart attacks.[38]

Table 05 :- Animal venom derived products in modern healthcare

D] Case Studies: Modern Drugs Derived from Natural Sources :-

This revolution from traditional remedy to modern pharmaceuticals led to the discovery and development of many life savers drugs. Many of these medicines originated from natural sources, like plants, fungi, and more; they have been developed into lifesaving treatments currently in use. Some of the relevant examples of modern drugs obtained from natural sources are as follows:

I) Aspirin (Acetylsalicylic Acid): Derived from Willow Bark :-

It is still among the most frequently used medications worldwide, first extracted from willow bark (Salix alba). However, early civilizations were aware of how to make it use to get rid of pain and inflammation as many did, Egyptians and Greeks by chomping on willow bark. In 1897, scientists at Bayer isolated acetylsalicylic acid, a more stable, less irritating form of salicin, which is the active ingredient in willow bark. Today, aspirin is prescribed not only for analgesic and anti-inflammatory purposes but also for its cardioprotective properties in the prevention of heart attacks and strokes.[39]

II) Artemisinin: Originated from Sweet Woodruff :-

The potent antimalarial drug artemisinin comes from the tiny plant known as sweet wormwood or Artemisia annua. Artemisinin was rediscovered in the 1970s by Chinese scientist Tu Youyou as she sought treatments for malaria; it has proven effective against the Plasmodium species-the parasite-causing malaria, particularly when other drugs had caused resistance to build up in the parasite. Its strong action and low toxicity have made it the backbone of combinations therapies in treating malaria, saving millions of lives around the world.[8]

III) Penicillin: Derived from Fungus :-

Penicillin, isolated by Alexander Fleming in 1928, is produced by mold known as Penicillium notatum. The antibiotic revolutionized the practice of medicine because a cure now existed for what otherwise became fatal diseases such as pneumonia, syphilis, and strep throat. Penicillin functions as an inhibitor of bacterial cell wall synthesis; it is thus bacterially antagonistic to all pathogenic species of bacteria. The discovery of penicillin has been the threshold to the antibiotic age, and the resultant antibiotics up to date have been developed.[31]

IV) Paclitaxel (Taxol): Derived from Pacific Yew Tree:-

The anticancer drug Paclitaxel, or Taxol, was first isolated from the bark of the Pacific yew tree, Taxus brevifolia. This drug causes the death of rapidly dividing cancer cells by interfering with the normal function of microtubules during the division of a cell. It is widely used for ovarian, breast, and lung cancers. With the discovery of paclitaxel, plant-based compounds were placed high on the list to be looked into further concerning their use in cancer treatment; its synthesis has since been modified to yield higher quantities and sustainable uses.[41]

V) Lovastatin: Originated from Fungus:-

Lovastatin is a cholesterol-lowering drug that has been isolated since the 1970s from the fungus Aspergillus terreus. Lovastatin is a statin type of drug, meaning it acts on the enzyme HMG-CoA reductase during cholesterol synthesis. Lovastatin, thereby reducing cholesterol levels, prevents cardiovascular diseases like heart attacks and strokes. Lovastatin, like other statins, is a drug in today's pharmacopoeia that is among the most prescribed worldwide and reflects the importance that natural products place in the management of modern health problems.[42]

VI) Ivermectin: Derived from Soil Bacteria:-

Ivermectin is a bacterium of the type Streptomyces avermitilis, which was discovered in the 1970s and has been used for the treatment of parasitic infections, including river blindness or onchocerciasis and lymphatic filariasis. In the treatment, ivermectin paralyzes and kills the parasites, thus furnishing a highly effective and low-cost treatment. Ivermectin had significantly impacted public health, especially in the tropics in which the parasitic diseases are endemic.[43]

4. Mechanisms of Action of Natural Products:-

A] Biological Activities:-

The biological activities of natural products vary widely and are a contributory factor to their therapeutic potential. Most compounds belonging to these categories act through specific biochemical pathways that enable them to perform a variety of roles, including acting as antioxidants, anti-inflammatories, anticancer agents, and antimicrobials, among others. We now discuss the primary mechanisms of action of natural products and their related biological activities.

I) Antioxidant Activity:-

Antioxidants are compounds that neutralize free radicals and ROS through the prevention of undesirable effects of oxidative stress leading to cellular damage and diseases like cancer, cardiovascular diseases, and neurodegenerative disorders. In this sense, many natural products contain a rich amount of antioxidant compounds, such as polyphenols, flavonoids, and vitamins.

Mechanism:- The antioxidant compounds scavenge ROS by the donation of electrons to neutralize free radicals without themselves getting reactive. They also upregulate the antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase in cells to protect cells from oxidative damage.[49]

Example:- The polyphenol quercetin, extracted from fruits and vegetables has been shown to scavenge free radicals and reduce oxidative stress.[47]

II) Anti-inflammatory Activity:-

Inflammation is a physiologic response to infection or injury but chronic inflammation plays a role in diseases like arthritis, cardiovascular disease, and even cancer. The modulation of the immune response by natural products with an anti-inflammatory effect through the regulation of important signaling pathways reduces the inflammatory effect.

Mechanism:- Many of the naturally occurring compounds inhibit the nuclear factor-kappa B (NF-κB) pathway, which modulates the production of pro-inflammatory cytokines. Others counteract COX enzymes, particularly COX-2, implicated in the biosynthesis of inflammatory mediators including prostaglandins.[21]

For instance, curcumin is a plant-derived compound which is strong anti-inflammatory, extracted from Curcuma longa, also called turmeric. This agent could suppress the activation of NF-κB in such a way that it leads to reduced production of inflammatory cytokines.[23]

III) Anticancer Activity:-

Natural products have been of immense promise in anticancer research due to their capabilities in inhibiting cell growth in tumors, causing apoptosis or programmed cell death, and preventing metastasis. Many anticancer natural compounds are known to inhibit cellular processes related to the development of cancer.

Mechanism:- These molecules can activate the intrinsic, or mitochondrial, as well as the extrinsic, or death receptor pathway of apoptosis. Others function by controlling cellular growth through cell cycle arrest at various checkpoints. Some also inhibit neovascularization or the generation of new blood vessels, which supply a tumor, or induce autophagy where dysfunctional cells are removed.[2]

Example:- Paclitaxel, an anticancer drug which is obtained from the bark of the Pacific yew tree, Taxus brevifolia, has the ability to stabilize microtubules and block their disassembly, thereby interrupting cell division through a signal to apoptosis in cancer cells.

IV) Antimicrobial Activity:-

Many natural products possess antimicrobial properties, making them useful in combating bacterial, viral, fungal, and parasitic infections. These compounds either kill pathogens directly or inhibit their growth and replication.

Mechanism:- Antimicrobial natural products disrupt cell membrane integrity, inhibit essential enzymes, or interfere with nucleic acid synthesis. Some also enhance the immune response to eliminate pathogens For example, natural antibiotics like penicillin inhibit bacterial cell wall synthesis.[45]

Example:- Garlic (Allium sativum) contains allicin, a compound with broad-spectrum antimicrobial activity that works by disrupting microbial cell membranes and inhibiting key enzymes.[44]

V) Cardioprotective Activity:-

Natural products contribute to cardiovascular health as they help reduce blood pressure, cholesterol levels, and even prevent atherosclerosis. The majority of these compounds enhance endothelial function and offer protection against oxidative stress, and are involved in lipid metabolism modulation.

Mechanism:- Cardioprotective compounds, including polyphenols, act via the improvement of endothelial function and decrease in inflammation in blood vessels, also the lower oxidative stress. They also maintain lipid metabolism by way of regulation of the enzymes which participate in cholesterol synthesis (such as HMG-CoA reductase).[50]

Example:- Resveratrol is a phenolic compound present in grapes and red wine and has influence on vascular functions through activation of nitric oxide synthase and by reduction of oxidative damage.[46]

VI) Neuroprotective Activity:-

Natural products have gained much attention through their neuronal protective capabilities, through which they can prevent neurons from being destroyed and, thereby, reduce the risk of neurodegenerative diseases such as Alzheimer's and Parkinson's.

Mechanism:- These natural products reduce oxidative stress, inhibit neuroinflammation, and have been found to prevent the formation of misfolded proteins. Many scientists consider these hallmarks of neurodegenerative diseases. Other substances are known to improve synaptic plasticity and neurogenesis, which relate directly to brain function and cognitive health.[48]

For instance, flavonoids and terpenoids found in the extract of Ginkgo biloba enhance memory and cognitive functions by augmenting blood flow to the brain aside from exerting antioxidant activity.

B] Synergy with Modern Drugs: Enhancing Efficacy and Reducing Side Effects:-

The synergy of natural products in combining them with modern synthetic drugs has been receiving more and more attention over the years in medical research. When natural products are used in combination with conventional pharmaceuticals, they complement the therapeutic outcome through improved efficacy of the drugs, reduced drug resistance, and reduced adverse side effects. The synergistic approach presents multiple advantages in the treatment of complex diseases such as cancer, infectious diseases, and metabolic disorders.

I) Enhanced Efficacy:-

A combination of a natural product with a synthetic drug can potentiate the therapeutic effects of both agents. It is often said that this would be synergy, where the combined action is greater than that of the sum of both the individual effects. Natural compounds can target various targets or pathways, complementing the mechanism of action of synthetic drugs.

Mechanism:- Natural products can interact with drug targets, increase the absorption or bioavailability of drugs, and inhibit drug-metabolizing enzymes, which all contributes to greater effectiveness of drugs. Some

natural compounds may also sensitize cells to synthetic drugs, especially for anticancer and antimicrobial treatments, which further increases the response to drugs.

Example:- Curcumin, the active principle of turmeric, the active compound responsible for its activity, has been shown to enhance the activities of chemotherapeutic agents like 5-fluorouracil and paclitaxel through its anti-proliferative and pro-apoptotic activities. The drug dosages are lessened with enhanced clinical outcomes as a result of combining the drugs.[94]

II) Reduced Drug Resistance:-

These, in general, can overcome or delay drug resistance, especially with infections and cancer. Synthetic drugs pose a major challenge to modern medicine in relation to the development of resistance, and combining these drugs with natural compounds helps in a multi-targeted approach against prevention or combating resistance.

Mechanism:- Natural products can inhibit the efflux pumps that cause drug resistance in bacteria or in cancer cells. This is also capable of downregulating resistance-related genes' expression or modulating the microenvironment, making it hard for pathogens as well as even cancer cells to adapt.[53]

Example:- Berberine, the alkaloid extracted from various plants, for instance Berberis vulgaris, reveals promising potential for overcoming multidrug resistance by the inhibition of P-gp efflux pumps which remove drugs from cells, thereby enhancing chemotherapy.

III) Minimizing Side Effects:-

One of the many advantages of using natural products in combination with synthetic drugs is the possible reduction of side effects attributed to conventional treatments. Allowing for less aggressive or protective effects may simply mean that a natural compound can alleviate the tolerance and quality of life of a patient by itself.

Mechanism:- Natural compounds are rich in antioxidants or anti-inflammatory activities that might reduce the adverse effects or toxicity of synthetic drugs. For example, some antioxidants from natural origins can shield the body from oxidative stress from certain chemotherapy drugs.[54]

Example:- The milk thistle plant (Silybum marianum) derivative called silymarin has remarkable hepatoprotective properties. As an example of reduction factors, silymarin can be applied to the reduction of liver toxicity that patients suffer from under chemotherapy or when taking drugs with known adverse effects on the liver.[55]

IV) Improved Bioavailability:-

These natural compounds enhance the bioavailability of synthetic drugs, so that they are effective at lower doses than otherwise required. Poor solubility and rapid rates of metabolization are a problem to many drugs.

Mechanism:- Some natural products act as inhibitors of the cytochrome P450 enzymes, which are responsible for the metabolism of drugs to be broken down in a lesser manner and delay their action in the body. Others enhance drug absorption by altering membrane permeability or by aiding drug crossing across cellular barriers.

Example:- The alkaloid piperine in black pepper, Piper nigrum inhibits CYP enzymes and P-gp and increases the bioavailability of drugs such as curcumin and a few antibiotics even at a low dose.[52]

V) Broadening Therapeutic Window:-

This will make it possible to expand the therapeutic window-the dosages at which a drug is effective without inducing toxicity. Natural compounds might protect healthy cells, making it plausible for synthetic drugs to selectively target diseased cells.

Mechanism:- Since natural products may selectively guard non-diseased tissues against the cytotoxic side effects of synthetic drugs, the drugs' active and toxic doses are increased. They may also modulate immune responses, ensuring that the efficacy of immune-based therapies is enhanced without enhancing the risk for adverse effects.

Example:- Quercetin, a flavonoid of fruits and vegetables, has been shown to protect the normal tissues from the cytotoxic effects of radiation therapy and chemotherapy while enhancing cytotoxic effects on cancer cells, therefore opening the therapeutic window.[51]

5. Role in Drug Discovery:-

A] Screening of Natural Products:-

Natural products have been a vital part of discovery for centuries. They act as the sole source of novel bioactive compounds that can be used to find novel therapeutic agents. This is, therefore, performed through

a set of methodologies aimed at screening pharmacologically active compounds derived from natural sources. This set of methodologies combines traditional knowledge, high-throughput screening technologies, and advanced analytical tools in order to isolate, characterize, and evaluate bioactive compounds.

I) Traditional Knowledge-Based Screening:-

This basic knowledge of the medicinal plants and natural remedies forms the foundation for selecting the initial natural products in drug discovery. The ethnobotanical studies, coupled with ethnopharmacological information, assist investigators who would like to select plants, marine organisms, and other sources that have been conventionally used for medicinal purposes.

Methodology:- Ethnobotanical studies include collecting and recording traditional knowledge on medicinal plants, which in turn is applied to pick species for further screening, pharmacologically.[61] Such traditional healers and local practitioners offer clues on possible uses of certain plants or natural products that are later supported by scientific validations.

For instance, discovery of artemisinin from Artemisia annua, also known as sweet wormwood, for the treatment of malaria is just one example of how drug discovery is based on traditional Chinese medicine practices.[8]

II) High-Throughput Screening (HTS):-

High throughput screening is a highly potent method to screen thousands of samples against a target or disease model in a very short time frame for any potential biological activity of large libraries of natural product extracts.

In HTS, an in vitro screening of the extracts or fractions of natural products is undertaken using automated platforms that permit testing for modulating biological targets such as enzymes, receptors, or ion channels. In this sense, HTS typically employs complex assays such as cell-based assays, biochemical assays, or reporter gene assays that ensure detection of such biological activity.[64] Usually, the process gives "hit" compounds, which are then developed and optimized.

Example:- HTS has been used to identify bioactive compounds from marine sponges that later resulted in anticancer drugs such as discodermolide, a potent microtubule-stabilizing agent.

III) Bioassay-Guided Fractionation:-

Bioassay-guided fractionation is one of the paramount tools of natural-product drug discovery. It involves keeping track of the activity of an extract through successive steps of fractionation and isolation to eventually identify the active compound(s).

Methodology:- A crude extract is prepared first from a natural source, such as a plant, marine organism, or microorganism. Then the extract is fractionated using liquid-liquid extraction, column chromatography, or even HPLC. Each of the fractions is subjected to specific bioassays, and active fractions are further fractionated until the pure bioactive compound is isolated.

Example:- Paclitaxel (Taxol) was isolated from the bark of Taxus brevifolia through bioassay-guided fractionation when cytotoxic activity against cancer cells was followed by the identification of the active compound.[41]

IV) Metabolomics and Dereplication:-

Metabolomics and dereplication are important in the context of natural product screening to avoid rediscovering known compounds and to channel attention onto the discovery of new bioactive substances. These methodologies are making use of sophisticated analytical tools in profiling chemical diversity related to natural products, and they easily identify active compounds.

Methodology:- Metabolomics is described as the comprehensive analysis of small molecules, also known as metabolites, in natural product extracts. The creation of metabolite profiles is facilitated through techniques including NMR spectroscopy, MS, and LC-MS. Dereplication refers to the identification of known compounds at the early stages of screening through comparison with existing spectral data in databases. This helps in the streamlining discovery by making it concentrate on novel compounds.

Example:- LC-MS-based metabolomics analysis enables new antimicrobial compounds derived from soil-dwelling bacteria to be identified directly with no need for prior isolation of known antibiotics .[63]

V) Computational Approaches (In Silico Screening):-

Naturally, as a result of new computational methods, screening of natural products is increasingly gaining importance. In silico screening is a form of screening that uses bioinformatics and cheminformatics resources to predict the biological activity of compounds in vitro before laboratory-based testing.

Methodology:- Molecular docking, virtual screening, and QSAR models comprise the most traditional computational methods. Such approaches utilize information relating to a molecule's chemical structure in an effort to predict interactions between natural compounds and biological targets. In silico screening reduces vastly the time and efforts required for experimental testing since it filters large compound libraries through towards the most promising candidates.

Example:- Molecular docking has been applied in the prediction of binding affinity of natural products, flavonoids and alkaloids, to key proteins involved in diseases, like cancer and Alzheimer's disease .[65]

VI) Microbial and Marine Natural Product Screening:-

Microorganisms, including bacteria and fungi, and even marine organisms, are copious producers of new bioactive compounds. Screening efforts thus include secondary metabolites of these organisms with characteristic interesting biological activities.

Methodology:- Screening by microbes entails the growth of microorganisms under selective conditions that may favor the production of secondary metabolites. Marine natural product screening involves the extraction and testing of compounds from marine organisms that include sponges, corals, algae that produce bioactive molecules, such as biota.[66] Active extracts are tested in various biological assays, and active compounds are isolated and characterized.

Example:- The great numbers of tested species of Streptomyces result in antibiotics, from which invention came life-saving drugs, such as streptomycin - a treatment for tuberculosis.[59]

B] Challenges in Drug Development: Standardization, Dosage, and Reproducibility in Natural Products:-

Although natural products are a rich source of modern drugs, the development of drugs from natural products faces a lot of challenges. Some of the main problems are standardization, dosage determination, and reproducibility. These considerations form a big challenge in the incorporation of natural compounds into modern therapies. Overcoming these challenges will be essential to ensuring the safety, efficacy, and consistency of therapeutics derived from natural products.

I) Standardization of Natural Products:-

Standardization:- The process in which there is an assurance that a natural product or extract contains the same concentration of bioactive compounds. This is among the most significant challenges in natural product drug development since the concentration of the active ingredients changes due to many factors such as material source, environmental conditions, and extraction methods.

Challenge:- The source of natural products from plants, animals, or microorganisms is sometimes characterized with quite high variability in chemical composition. Thus, pharmacological effects due to such products are occasionally inconsistent because of different concentrations of various bioactive compounds influenced by geography, climate, soil condition, and the time of harvest.The challenge here is the inability to attain uniformity in any drug formulation since it may result in non-uniform variations in clinical settings concerning reproducibility and safety.

Solution:- Advanced techniques such as HPLC, MS, and NMR characterize and determine the quantitative amount of the active components in natural products. Thus, the batches of such a natural product are ensured to have bioactive content with good consistency.

Example:- Standardization of extracts of the most commonly used ginseng species, Panax ginseng, is largely based on determination of ginsenoside content, and such standards are used to vary percentages of ingested ginsenosides in commercial products.

II) Dosage Determination:-

A major task in the determination of appropriate dosage with natural products is that their chemical composition can be very complicated; chemical constituents in a natural product may be many and have various numbers of bioactive constituents which can interact with each other. The pharmacokinetics of synthetic drugs, on the other hand, is mostly constituted by one compound.

It is very difficult to define the dose-response relationship in natural products due to the presence of many active and inactive compounds in such products. The optimal dosage also depends on the age, weight, genetics, and health status of the patient. Traditional medicine practices, once again, have a different effect from those that have been applied in modern therapeutic applications with regards to formulation and preparation.[14]

Preclinical and clinical studies are required to document safe and effective dosing levels of natural products. Such studies also define the pharmacokinetic profiles, including ADME parameters. Advanced formulation

methods applied to natural product-derived drugs, such as nanoencapsulation, may increase their bioavailability and controlled release, hence enabling control over the dosage given more accurately.

Example:- Curcumin is a spice molecule derived from the plant Curcuma longa and has poor oral bioavailability. However, liposomal curcumin and curcumin-piperine preparations have been formulated to increase absorption, hence to exert greater therapeutic efficacy at lower doses.[67]

III) Reproducibility of Results:-

Reproducibility is a challenge in natural product research. Reproducibility is considered as consistency between different studies or batches of the same natural product to give related results. Inconsistencies may be partly due to source material variation, differences in extraction methods and variation in composition complexly posed in natural products.

Challenge:- The pharmacological effect is not reproducible in natural product-based research because of variability in raw material and differences in extraction method, among other reasons, and the presence of multiple bioactive compounds. It has remained one of the major hindrances to the clinical development of natural products because regulatory agencies require consistent results before new drugs are approved.[15]

High reproducibility may thus be achieved by setting up standard protocols governing the collection, processing, and testing of natural products. These may include standardization of GACP, followed by plant material, standardized extraction techniques, and standardized fractionation techniques. There should also be the development of standard methods in bioassays and chemical profiling to bring together uniform experimental results.[53]

Example:- Results of studies of the medicinal herb used to treat mild to moderate depression called St. John's wort, Hypericum perforatum, can be reproduced better since the consistent extraction procedures with standardized procedures ensure that the extract will have hypericin levels constantly.

IV) Regulatory and Quality Control Challenges:-

The legal and regulatory situation is very complex and region-specific, and detailed testing of the safety, efficacy, and quality of natural products is necessary before their approval for use by agencies like the U.S. Food and Drug Administration and the European Medicines Agency. However, this is rather challenging because of the complexity of mixtures of natural products.

Challenge:- There is an inability to have a defined protocol for getting natural products accepted as drugs, thus making it difficult for them to be utilized in mainstream medicine. Mostly, the natural products are labeled as dietary supplements rather than pharmaceutical agents. This would naturally receive much less scrutiny than should be for such an agent, which adversely impacts its quality control aspect, safety, and efficacy.

Solution:- Natural products require uniformity in their regulation across nations and must have quality control standards for their production and testing. Growing awareness of natural products and their potential is realized through this recognition. Companies are now asked to go by guidelines prescribed by the registration authorities, which include clinical trials, standardized manufacturing, and post-market surveillance for the allowance of these natural products as therapeutic agents.[14]

Example:- Botanical drug The botanical drug Veregen (sinecatechins), an extract of green tea for the treatment of genital warts, was accepted by the FDA as a prescription drug after rigorous tests of its clinical safety and quality control.

V) Sustainability and Supply Chain Issues:-

Another challenge in drug development is ensuring the supply of pharmaceuticals derived from natural products. Over-harvesting, habitat destruction, and climate change are potential issues that could threaten the availability of natural resources used as medicinal sources.

Problem:- Many natural products originate from species that are threatened or are endemic to a small geographic area, which raises the specter of sustainability and ethical concerns. In addition, the dynamics within the supply chains will lead to fluctuations in the availability and quality of raw materials for natural products.

Solution:- Besides, sustainable harvesting practices, cultivation of medicinal plants, as well as biotechnological approaches, such as microbial fermentation and plant cell culture, are developed for keeping a consistent and sustainable supply of natural products. Biotechnology can also provide alternative sources of bioactive compounds, which could be produced in controlled environments.[1]

Example:- Cultivation of Taxus species has been used as an alternative to harvesting from wild yew for the production of paclitaxel, an anti-cancer drug which was originally obtained from wild yew trees.[72]

C] Success Stories: Transition of Natural Products into Modern Medicines:-

Natural products still constitute a very important source of drug discovery. Many natural compounds have been developed into therapeutic agents, which provide quite effective treatments for a number of diseases. The following is a list of some of the best-known natural products developed into widely used modern drugs:

I) Paclitaxel (Taxol) : Cancer Treatment:-

A drug exemplified most powerfully the strength of natural products in cancer therapy was paclitaxel. The bark of the Pacific yew, Taxus brevifolia originally contains it. In the 1960s, a screening program by the U.S. National Cancer Institute discovered it, and from there it entered into the chemotherapy cabinet as one of its more effective chemotherapeutic agents.

Mechanism:- Paclitaxel acts by stabilizing microtubules; with this action, it prevents the depolymerization of microtubules during cell division; it therefore inhibits the proliferation of cancer cells.

Clinical Use:- It is a treatment for different kinds of cancers such as ovarian cancer, breast cancer, lung cancer, and pancreatic cancer.

Impact:- The discovery and development of paclitaxel have resulted in finding alternative supply chains in plant cell culture and semi-synthesis from related species which has ensured sustainability of this drug.[72]

II) Artemisinin: Malaria Treatment:-

Artemisinin was the first to be identified in the 1970s by a Chinese scientist, Tu Youyou, from the sesquiterpene lactone of Artemisia annua, commonly known as sweet wormwood. Considering presently available ACTs as the future gold standard of treatment for malaria caused by Plasmodium falciparum, especially in drug-resistant regions, the need for understanding the biology of the malaria parasite cannot be overemphasized.

Mechanism:- Artemisinin generates ROS in the cells of the parasite, thus interfering with its life cycle and resulting in the death of the malaria parasite.

Clinical Use:- It is used globally in ACTs for the treatment of malaria, particularly in drug-resistant cases.

Impact:- The millions of lives artemisinin has saved in Africa and Southeast Asia have earned its discoverer, Tu Youyou, the Nobel Prize for Physiology or Medicine in 2015.

III) Aspirin (Acetylsalicylic Acid): Pain and Cardiovascular Treatment:-

The first aspirin in the world, one of the most known drugs, is obtained from salicin, a compound present in willow bark (Salix species). Many ancient civilizations may be known to have used willow bark for its analgesic properties. In the 19th century, scientists synthesized acetylsalicylic acid, a more stable form of salicin, which later became the modern drug aspirin.

Mechanism:- Aspirin inhibits the activity of the enzyme cyclooxygenase, resulting in the diminution of prostaglandins responsible for the mediation of pain, inflammation, and fever. In addition, aspirin exerts an antiplatelet effect, which renders it useful for preventing heart attacks and strokes.[74]

Its clinical applications are for pain relief, for anti-inflammatory therapy and as preventive medicine against cardiovascular diseases.

Impact:- Aspirin is one of the most frequently prescribed medications for the pain and the heart. The development of aspirin represented one of the largest successes in history regarding the migration of traditional remedies into modern therapeutic agents.

IV) Penicillin: Antibiotic:-

Penicillin, from the fungus Penicillium notatum was discovered by Alexander Fleming in 1928. It became the first of the fairly usable antibiotics and marked a turning point in the treatment of bacterial infections.

Mechanism:- Penicillin inhibits the formation of cell walls of a bacteria through interference with peptidoglycan, resulting in cell lysis and death of the bacterium.[75]

It is used to treat various sorts of bacterial infections, including pneumonia, strep throat, and syphilis.

Impact:- The discovery of penicillin marked the beginning of the antibiotic era that resulted in markedly reduced mortality and morbidity from bacterial infections, firmly placing it on the list of critical drugs in modern medicine.

V) Lovastatin: Cholesterol-Lowering Drug:-

Lovastatin, isolated from Aspergillus terreus, is one of the earlier statins developed specifically for reducing cholesterol. Lovastatin, like several other statin drugs, acts by inhibiting the enzyme HMG-CoA reductase, which is localized in the liver and catalyzes the synthesis of cholesterol.

Mechanism:- Lovastatin works as a drug used for cholesterol-lowering medications by inhibiting the HMG-CoA reductase enzyme, which then leads to lower cholesterol production and more uptake of LDL from the blood.[76]

Clinical Use:- It has been used in treating hypercholesterolemia followed by the prevention of cardiovascular diseases.

Impact:- Lovastatin and other statins have become the cornerstone of drug therapy in atherosclerosis and cardiovascular disease, dramatically reducing the number of heart attacks and strokes.

VI) Morphine: Pain Management:-

Developed from the opium poppy (Papaver somniferum), morphine has been used over the past centuries to relieve severe pain. Isolated for the first time in the early 19th century, morphine was taken as a standard by which all the other pain medications were judged, especially in the case of severe or chronic pain conditions.

Mechanism of Action:- Morphine functions as an agonist on opioid receptors. It primarily influences the perception and responses to pain by binding to the mu-opioid receptors in the brain and spinal cord.[78]

Clinical Use:- For severe pain associated with surgical, traumatic, or malignant conditions.

Impact:- Morphine is significantly used despite the dangers of addiction and dependency to manage pain in palliative care and surgery.

6.Integration of Traditional Medicine in Modern Healthcare:-

A]Complementary and Integrative Medicine:-

More recent concepts, since there is significant interest in the intersection between traditional medicine and conventional medicine. In fact, this effort is known as the area of Complementary and Integrative Medicine (CIM), combining conventional and less conventional approaches to health care with diverse approaches and methods, offering holistic treatment for chronic diseases such as cancer, diabetes, and heart disease. It is based on enhanced awareness of the contribution traditional medicine can give to improving therapeutic results, quality of life, and overcome the limitations of modern medicine.

I) Cancer Treatment:-

Apart from surgery, chemotherapy, and radiation, cancer treatment encompasses the three approaches together. These treatments are very effective but carry side effects, including fatigue, pain, nausea, and immunosuppression. Combining CIM with traditional medicine in cancer care has been known to benefit patients by managing symptoms, enhancing quality of life, and also augmenting effectiveness of conventional treatments.

Traditional approaches: Most cancer patients seek to apply herbal medications, acupuncture, and mind-body practices such as yoga and meditation. For example, TCM formulas, including herbal preparations like Shenqi Fuzheng and Astragalus supplements, have been documented to help with immune stimulation as adjunctive care during chemotherapy treatment and decrease the associated treatment fatigue.[79]

Implication on Treatment: The outcomes from systematic reviews generally establish the effectiveness of acupuncture therapy in treating chemotherapy-induced nausea and vomiting and pain management in cancer patients.[80] In addition, mind-body therapies have been established to help reduce stress and enhance the emotional well-being in cancer patients.

II) Diabetes Management:-

The use of herbal remedies to regulate blood glucose levels has long been practiced in many traditional systems of medicine throughout the world. Diabetes is one of the most universal global health issues, and there is increasing interest in the use of these remedies in conjunction with conventional medicines in enhancing blood sugar control, improving insulin sensitivity, and preventing complications.

Allopathic drugs: Both Ayurveda and TCM have been in use for ages to treat diabetes with plant medications. For example, bitter melon-Momordica charantia, fenugreek-Trigonella foenumgraecum, and the berberine-containing extracts of Coptis chinensis are documented as having hypoglycemic activity.[81]

Impact on Treatment: Several studies now illustrate the ability of these herbs to suppress fasting blood glucose as well as enhance the level of sensitivity toward insulin when used in combination with standard anti-diabetic drugs such as metformin. In this regard, berberine has gained much attention concerning its potential to help regulate glucose metabolism and the subsequent reduction in insulin resistance in patients with type 2 diabetes.

III) Heart Disease Prevention and Management:-

Heart disease is still considered the leading cause of death worldwide, but the management of the condition does not only end with lifestyle modification, medications, and, in some cases, surgery, but is now increasingly integrating some traditional medicine approaches into the prevention and management of heart disease, mainly concerning its risk factors: high cholesterol and hypertension, and inflammation.

Traditional Medications: Other medicinal herbs include red yeast rice (Monascus purpureus), garlic (Allium sativum), and hawthorn (Crataegus species) for controlling cardiovascular well-being. Historically, red yeast rice has been used because of its content of statins. This will result in lowering the levels of cholesterol. Hawthorn on the other hand was applied to improve heart functionality using reduced levels of blood pressure.[83]

Impact on Treatment: Traditional remedies can become synergistic with conventional drugs in treating patients with hypertension and cholesterol. Thus, studies by Becker et al. demonstrated that red yeast rice is equivalent to low doses of statins in reducing LDL cholesterol, with fewer adverse effects (2009). Haworth extract increased exercise capacity and reduced blood pressure in heart failure patients, thus concluding.[85]

IV) Chronic Pain Management:-

Not only does chronic pain resulting from arthritis, back pain, and fibromyalgia bring about disability in its wake around the world, but incorporating traditional medicine-like acupuncture and herbal remedies into current pain management makes the arsenal of treatments available today all that much deeper.

Conventional Medicinal Interventions: Acupuncture is one of the most important practices in TCM in the management of chronic pain, especially among musculoskeletal pain conditions. Herbal medicines-curcuma longa and Zingiber officinale-are also used for their anti-inflammatory properties.[86]

Impact on Treatment Acupuncture is now commonly prescribed in pain clinics to be used as an adjunct to traditional pain management. The efficacy of acupuncture treatment has been confirmed with evidence showing that many patients with chronic pain receive great relief with fewer side effects from acupuncture than pharmacological treatments.[87] Integrative approaches for arthritis and other inflammatory conditions are beginning to include the anti-inflammatory effects of turmeric and ginger.

B] Global Recognition: WHO's Role in Promoting Traditional Medicine in Global Health Policy:-

The WHO played a crucial role in recognizing and promoting traditional medicine as an essential ingredient of global health policy. In the last decades, WHO has actively lobbied for the integration of traditional medicine into national healthcare systems, not least in regions where traditional practices are important components of the healthcare culture. That recognition has proven to be the key in providing access to the old knowledge on medication and safe use along with the modern systems of healthcare.

I) WHO Traditional Medicine Strategy:-

In 2002, WHO launched its first Traditional Medicine Strategy (2002–2005) to promote the development and integration of traditional and complementary medicine within national health systems. The strategy was further expanded by WHO's Traditional Medicine Strategy 2014–2023 that will ensure the development of a holistic framework for integrating traditional medicine into healthcare, making sure that patients benefit from this rich diversity of safe and effective treatment options.[88]

Key Objectives:-

Support its member countries in developing policies and regulations that assure the safety, effectiveness, and quality of traditional medicine.

Promote evidence-based research on traditional medicine to ensure its authenticity for therapeutic use and improve its implementation in healthcare.

Promote the inclusion of traditional medicine in medical training and education.

II) Global Traditional Medicine Database and Knowledge Sharing:-

The WHO has also stressed the need for mutual exchange of knowledge and a universal database of traditional medicine. In doing so, it collaborates with member states to develop systems capable of documenting the wealth of diversity of practices in traditional medicine for the safeguarding of indigenous knowledge as well as its access for research and development purposes.

For example, the WHO's Global Centre for Traditional Medicine, which it partnered with India to roll out the global platform, serves as a knowledge point for practices related to traditional medicines across the globe. Such a center works at developing evidence-based research with a repository on traditional therapies and herbal medicines contributing to global health innovation.[89]

III) WHO's Role in Promoting Safety, Quality, and Regulation:-

WHO argues that traditional medicine must be regulated for safety and efficacy. It engages countries in building national policies, safety, and quality standards, and formal regulatory frameworks for the products of traditional medicines. Particularly, it has been noted that in herbalism, the most popular form of practice, there is not much standardization in terms of manufacturing and dosage.

Guidelines developed by WHO to assist countries in the assessment of the safety and efficacy of traditional medicine, Guidelines for the Assessment of Herbal Medicines, which assumes a scientific basis for assessing traditional therapies in the context of modernity. All this has provided an impetus toward safer use of traditional medicine products around the world.[90]

IV) Role in Universal Health Coverage (UHC):-

The WHO describes traditional medicine as a valuable resource toward attaining the 2030 goals of universal health coverage, especially among low and middle-income countries where modern healthcare services cannot be reached easily. WHO thus integrates traditional practices into public health systems towards acceding more healthcare and delivering culturally appropriate medical care.

This is the reason why the WHO is now preaching the integration of traditional medicine; there are various estimates indicating that around 80% of the population in many developing countries relies on traditional medicine for primary health care.[88] This is recognition of the importance of not pushing traditional medicine to a corner but mainstreaming it as a precious complement to modern medical practices.

C] Regulation and Standardization of Traditional Medicine: Ensuring Safety and Efficacy:-

Such use of traditional medicines is continuously on the increase, and, hence, regulation and standardization have become a global priority. It is crucial to guarantee safety, efficacy, and quality in any traditional medical practice and product meant to integrate with the mainstream modern healthcare systems. International organizations, for their part, such as the World Health Organization (WHO), and national regulatory bodies of countries, during the last few decades, have paid attention to the establishment of control frameworks for traditional medicine. A lot of attention in such efforts is focused on developing guidelines on product quality, dosage, clinical trials, and practitioner certification.

I) WHO's Role in Regulation and Standardization:-

WHO has played a frontline role in facilitating countries in achieving proper regulation and standardization of traditional medicine. Its General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine provides a worldwide guide in evaluating the safety and efficacy of traditional remedies. These guidelines facilitate harmonization of research methodologies and provide scientific approaches to TM practices by both the industrialized and developing countries.[90]

The WHO Traditional Medicine Strategy 2014–2023 encourages countries also to build suitable regulatory measures that will guarantee the safety and quality of traditional medicine products. The countries should implement Good Manufacturing Practices; labeling, dosage, and usage shall be well defined for herbal medicines.[88]

II) National Regulatory Frameworks:-

Countries like China, India, and Japan, which have had a long tradition of herbal medicine, have equally defined national country-specific frameworks to govern the practice of traditional medicine. For example, in China, SATCM provides quality and safety standards for TCM products supplied to the market. In the National Pharmacopoeia, TCM is classified as Class-one drug with well defined processes for its production, formulation, and clinical uses.

Besides, India's Ministry of AYUSH, Ayurveda, Yoga & Naturopathy, Unani, Siddha, and Homeopathy governs traditional medicine and has established regulations for clinical trials and qualification of practitioners. The Indian government has also made efforts to institutionalize herbal drug production by setting up bodies such as the Pharmacopoeia Commission for Indian Medicine & Homoeopathy, through the publication of standardized formulations of Ayurvedic medicines.[92]

III) Challenges in Standardizing Traditional Medicine:-

Even so, there is still a lot in terms of improvement in the regulation and standardization of traditional medicine, especially on its disparity on raw materials, no uniform dosage application, and complexity of multi-compound herbal formulation that makes quality control harder, especially if such efficacy depends on the combination or conditions for the cultivation and harvesting of these ingredients.

Raw Material Variability: Quality of herbal formulation can vary significantly because of climatic factors, harvesting technique, and storage. Standard methods for growing, harvesting, and processing must be set in place in order to deliver consistency of quality.[93]

Dosage and Clinical Validation: Traditional drugs hardly exist with clear dosages and clinical validation because they often bring uncertain results in treatment. This is the main reason why most traditional medicines now experience modern clinical trials and research to determine their safety, dosing, and efficacy in a controlled setting.[14]

IV) Pharmacovigilance and Safety Monitoring:-

Pharmacovigilance, in the context of ensuring the safety of medicines launched post-research, is increasingly being applied to traditional medicine. WHO encourages countries to include traditional medicines in their pharmacovigilance systems with a view to detecting and reporting adverse events. In India, for example, it has developed a specific arm for monitoring traditional medicine under its Pharmacovigilance Programme of India (PvPI) that monitors adverse drug reactions (ADRs) pertaining to traditional and herbal medicines.[95]

This ensures that traditional medicines included in pharmacovigilance systems are viewed early in terms of potential risks and that they can satisfy the requirement of safety standards applied to conventional medicines.

V) Good Manufacturing Practices (GMP):-

To ensure high quality products, Good Manufacturing Practices need to be followed. Application of GMP guidelines ensures that the product is manufactured in a consistent and controlled manner, thus ensuring safety, quality, and efficacy. WHO has formulated specific GMP guidelines for herbal medicines. Many countries have adopted such standards for manufacturers who produce traditional medicine products.[91]

Regulatory Adoption: China, India, and Japan adopt GMP standards in the preparation of traditional medicines wholly. For instance, the stringent measures that China has attached to TCM products have improved the quality and safety aspect of this TCM making it acceptable for use in most countries worldwide.

7. Ethnopharmacology and Bioprospecting:-

A] Ethnobotany and Ethnopharmacology in Drug Discovery:-

Ethnopharmacology and ethnobotany are interdisciplinary sciences that explore traditional knowledge to discover and validate new medicinal compounds derived from plants and other natural sources. Ethnobotany is the study of how a particular culture applies plants for medicinal, nutritional, and spiritual purposes. In turn, ethnopharmacology aims at understanding and scientifically validating the biological activities in those traditional remedies. There has been significant integration between indigenous knowledge and modern scientific methods in the identification of novel compounds that have advanced drug discovery and development.

I) Ethnobotany: Traditional Knowledge as a Resource:-

Ethnobotany-the use of indigenous plants by different cultures and locale-has been an important source in drug discovery. Most indigenous communities of the world possess knowledge spanning several centuries concerning medicinal plants. Traditional knowledge, therefore, acts as a guide in regard to which specific plants or remedies should be used, and then becomes subject to further scientific analysis.

For example, when the drug quinine, a malaria medication derived from the bark of the Cinchona tree was discovered, its knowledge originated from the traditional literature of an indigenous tribe in South America. Another instance is aspirin, a derivative from the Willow bark (Salix alba) is an example where traditional knowledge of the application of plants marks the precursor for modern pharmacology.[97]

II) Ethnopharmacology: Validation of Traditional Remedies:-

Ethnopharmacology is the extension of ethnobotanical research where science validates the biological effects of traditional remedies. Ethnopharmacological studies are conducted in conjunction with researchers to isolate active compounds from natural sources, explore their pharmacological mechanisms, and consequently develop them into some form of effective treatment.

For instance, artemisinin is an active component in the treatment of malaria, and it was isolated from the medicinal plant Artemisia annua. The herb has been used for decades in TCM for treating fevers. The story of artemisinin is a perfect example of how ethnopharmacology fills the gap between traditional medicine and modern pharmacology.[98]

III) Bioprospecting: The Search for New Drugs:-

With sustainable bioprospecting practices, over-harvesting risks and biodiversity loss risks are mitigated. Such practices include responsible sourcing, cultivation of medicinal plants, and adherence to international guidelines, as in the case of the Nagoya Protocol under the Convention on Biological Diversity (CBD). The Nagoya Protocol emphasizes fair and equitable sharing of benefits arising from the utilization of genetic resources, both monetary and non-monetary, for indigenous communities possessing traditional knowledge about those resources.[103]

Another sustainable form of bioprospecting is through the production of medicinal plants and marine organisms in culture rather than depend on them from the wild. An example in this area is successful breeding of species of Taxus for paclitaxel, which has partially reduced dependency on wild sources. Production of bioactive compounds through aquaculture is becoming a prominent feature in current marine biotechnology, which otherwise was destructive to the sensitive ecosystems of the sea.[104]

IV) In Situ Conservation and Ex Situ Cultivation:-

There are both ex-situ conservation of species in their habitats and in-situ cultivation of plants and organisms out of their native habitats, like cultivation in botanical gardens or laboratories. Each of the approaches proves very important for supporting biodiversity sustainability in the longer term.

In situ conservation: Natural habitats can be conserved through protected areas, either land. Such protected areas preserve biodiversity in case future bioprospecting might depend on it.

Ex Situ Cultivation: Growing medicinals and sea organisms in controlled situations reduces the need for wild collection. Botanic gardens, seed banks, and marine aquaculture facilities both serve to conserve species while providing scientists with a continuous supply of raw materials for drug development.[105]

V) Ethical Bioprospecting and Benefit Sharing:-

The ethical dimension of bioprospecting ensures that benefits derived from the exploitation of natural resources are shared with the communities and countries from which these resources have been sourced. In areas like indigenous knowledge, which the local communities have used for centuries, this is even more relevant. Under the Nagoya Protocol, there is stress on previous informed consent by indigenous communities and the fair share of profits derived from the commercialization of products, resulting from their knowledge. Ideally, the best bioprospecting project should accommodate agreements on base royalty, infrastructure development, and some capacity building for local communities aligned to support sustainable economic growth and environmental stewardship.

8. Challenges and Limitations:-

A] Scientific Validation of Traditional Medicines:-

One of the major impediments for traditional medicine in modern medical practice is the problem of scientific validation of its efficacy and safety, mainly because the majority of natural origin compounds are complex in preparation with many combinations difficult to characterize and select for single active compounds. Moreover, these treatments cannot be put into the modern medicine system without the use of large-scale clinical trials, standardized preparation, and quality control to ascertain its reliability and reproducibility.

I) Lack of Clinical Trials and Rigorous Testing:-

The dearth of well-designed clinical trials has been the main problem in the validation of traditional medicines. Oral tradition is the major tool for the transmission of traditional remedies, and many are not documented enough to match the parameters of the modern scientific research standards. Most traditional remedies are based on anecdotal evidence or a good few hundred years of empirical use, although they often are not submitted to the randomized controlled trials that serve as the foundation for the development of most modern drugs. Consequently, effectiveness and safety can only be very hard to establish, as well as optimum dosage without adequate randomized controlled trials.[107]

II) Standardization Issues:-

Standardization forms a significant impediment to the legitimation of traditional medicines. Traditional medicines are complex mixtures of various compounds whereas conventional pharmaceutical drugs are pure drugs with known concentrations. Its composition may change dramatically due to varying factors such as geographic location, environment, harvesting, and processing techniques. Therefore, consistency in the dosage, potency, and efficacy cannot be guaranteed.[108]

Such a lack of standardization in traditional remedy preparation makes it tough to reproduce the same therapeutic effects in different studies or even in different patients. Apart from this, differences in raw material

quality may also reflect differences in safety and efficacy, making it even more challenging to evaluate the clinical acceptability of traditional remedies.

III) Complex Mixtures of Compounds:-

Traditional remedies contain a lot of bioactive compounds, many of which work in synergy to produce the therapeutic effect. This potential for strength lends itself to not making it very easy to differentiate one active ingredient or predict the mechanism through which that compound might be acting. Little is known about the interactions between different compounds, nor does sometimes isolating particular compounds guarantee the full therapeutic effect as isolated from the rest of the remedy.

Moreover, traditional use of a whole plant or mixture of plants often ensures that some compounds will neutralize the side effects of others, a dynamic that is often overlooked when individual compounds are tested in isolation.[109] This gives difficulties in designing pharmacological studies to reflect accurately the traditional uses of such remedies.

IV) Regulatory Challenges:-

Another disturbing aspect in the validity of traditional medicine is an irregular pattern of standardized regulatory framework in various countries. While regulatory agencies show high standards demands toward testing of new drugs, this may not fit traditional medicine, which is not neatly classified into such categories. A remedy that has been used for hundreds or thousands of years might not even meet any requirements in a modern regulatory system that requires laboratory study and clinical trial results for evidence.

Traditional medicines are often marked as dietary supplements, while drugs are not. The same applies to pharmaceuticals which creates dangerous loopholes for different traditional products to enter and distribute in the market with concerns over their safety, efficacy, and quality control.[110]

V) Safety Concerns and Adverse Reactions:-

Although the assumption is generally that the old remedies are natural and so, safe, the assumption is usually misleading. With no scientific validation nor standardization, there is a risk of adverse reactions to happen, particularly if traditional medicines were taken along with conventional treatments. Moreover, there is also the danger of drug-herb interaction, contamination with toxic substances (e.g., heavy metals, pesticides), and incorrect dosages-all challenges which should be addressed by scientific study and regulation.

For example, there are some herbals associated with liver toxicity or renal damage; others alter the metabolism of conventional drugs, which may result in dangerous interactions. There is an urgent need to ensure that traditional medicines are safely accepted for use through scientific validation before incorporating them into modern health care systems.

B] Safety Concerns in the Use of Traditional Medicines:-

Traditional medicine has been on the rise in recent years, but it still possesses several safety issues. These include toxicity, adulteration, and interaction with conventional pharmaceuticals. Adverse reactions could be partly accountable for these concerns and health risks to public health. Consequently, there is a need to address the said concerns in offering traditional remedies as mainstream care.

I) Toxicity:-

Traditional remedies often consist of a complex mixture of various bioactive compounds that may be beneficial in some respects and toxic in others. For instance, some traditional medicines are derived from herbs with alkaloids, glycosides, or other phytochemicals known to have narrow therapeutic windows, such that any change in dosing may produce toxic effects. For instance, plants of the genus Aconitum contain drugs like aconitine, which are used in traditional Chinese medicine: with incorrect processing or improper administration they may manifest grave cardiovascular toxicity.[113] Other traditional herbal medicines have been linked with nephrotoxicity and oncogenic potential from chronic exposure like aristolochic acid-containing herbs.[114]

II) Contamination:-

Other major risks include contamination of traditional medicines. Pesticides, heavy metals such as lead, arsenic, or mercury may contaminate products due to poor quality controls at various stages in collection, processing, and production of traditional medicines. Some traditional herbal medicines contain poisonous levels of these hazardous substances, hence further posing serious health risks to consumers.[115] The impurities could be due to either the pollution in the environment or inappropriate production procedures that make it challenging to ascertain the safety of these products.

Other serious adulteration is the use of synthetic pharmaceuticals. Prescription drugs such as steroids, NSAIDs, or sildenafil are spiked into some traditional medicines to enhance their potency; unfortunately, this may be dangerous because the patients do not know if they have been given what they requested or what a combination of preparations may do for their health.[116.]

iii) Interactions with Modern Pharmaceuticals:-

There is one major concern of the use of traditional medicine in modern health care. That is the hazardous drug-herb interactions. Many patients utilizing some traditional remedies may also be prescribed prescription medicines; such herbs can interfere with the pharmacokinetics or pharmacodynamics of these drugs. For example, St. John's Wort (Hypericum perforatum), which is already known for depression remedy, acts on the cytochrome P450 enzymes, particularly CYP3A4, reducing the efficacy of drugs like oral contraceptives, anticoagulants, and some treatments of antiretroviral.[117]

The same has happened to ginseng and gingko biloba whose use interferes with blood thinners, like warfarin, thereby increasing the chances of bleeding or thrombosis.[118]

C] Ethical Issues: Biopiracy and the Protection of Indigenous Knowledge:-

With the increased use of natural products together with the traditional system of medicine in modern health care, huge ethical concerns arising still contain biopiracy and the protection of indigenous knowledge. It has been described as the exploitation of biological resources and traditional knowledge without due compensation or acknowledgment to indigenous communities that have nurtured and preserved these for centuries. Hence, ensuring fair and sustainable use of natural products in global healthcare systems becomes a critical task in response to such ethical concerns.

I) Biopiracy:-

Biopiracy is the situation in which corporations, researchers, or even countries use native resources and traditional indigenous knowledge without appropriately acknowledging ownership or sharing benefits. In many instances, the pharmaceutical company or institution puts a patent on compounds from plants, animals, or microorganisms used over generations in indigenous communities without adequately compensating them or giving credits.[119] This move not only denies indigenous communities their benefits but also disadvantages them culturally and traditionally.

One of the most famous cases of biopiracy is the patenting of the Neem tree by multinational corporations. For over two thousand years, Indian traditional medicine has used a plant called the Neem tree or Azadirachta indica for its medicinal, medicinal and pesticidal properties. Multinational companies attempted to patent Neem-based products in the 1990s without crediting knowledge Indian communities possessed; protests and lawsuits followed attempts to patent certain Neem-based product patents, some of which have been subsequently revoked.

II) Protection of Indigenous Knowledge:-

Oral communication has made indigenous knowledge systems prevalent and integral to a community's cultural identity. However, these knowledge systems still remain vulnerable to exploitation since they are not documented in ways recognized by international intellectual property (IP) laws. This leaves indigenous knowledge open to misuse by companies eager to commercialize traditional remedies without involving and compensating the communities that own this knowledge.[121]

There have been calls for stronger legal mechanisms, such as the Traditional Knowledge Digital Libraries, to document and safeguard traditional knowledge in order not to let it get into wrong use. Moreover, international agreements, like the Convention on Biological Diversity (CBD) and its Nagoya Protocol, highlight prior informed consent and a fair benefit-sharing agreement with indigenous communities each time their resources or knowledge is to be used for purposes of research and commercial development.[122]

III) Informed Consent and Benefit Sharing:-

Ethical research and development of natural products must involve the acquisition of prior informed consent from the communities where these resources and knowledge originate. This simply means that the indigenous groups must be fully informed of how such knowledge or resources will be used, and must agree to it before even beginning their research or commercialization. Further, these communities ought to be given a share of the benefits that accrue from their sources, either through monetary gain, development in infrastructure, or increased accessibility to health services.[123]

One of the successful examples is Hoodia gordonii, from where this plant of Southern Africa is specifically used by San people for the suppression of hunger during long hunts. The pharmaceutical companies developed

weight-loss products based on Hoodia's properties after disputes and legal settlements were made, and consequently, agreements were made to ensure the benefits accrue to the San people in commercializing Hoodia.[124] Such cases show that there is a necessity for fair benefit-sharing arrangements such that the rights of indigenous communities are respected.

IV) Legal and Policy Frameworks:-

Of course, preventing biopiracy and respecting indigenous knowledge, international actions have also been there. The developments brought about the most important policy changes-the Nagoya Protocol on Access and Benefit-Sharing, adopted under the Convention on Biological Diversity (CBD). As Tvedt & Young suggested, "the Nagoya Protocol recognizes the rights of indigenous and local communities to their genetic resources and traditional knowledge, requires prior informed consent over access, and provides for fair benefit-sharing" (2007). Such frameworks, however, are quite hard to fully implement in places with poor practices concerning the legal protection of indigenous communities.

9. Future Directions:-

A] Technological Advancements in Natural Products Discovery:-

With the rise in interest in natural products and traditional medicine by modern healthcare, technology has emerged as a crucial tool to expedite the discovery, refining, and development of bioactive compounds. Advances in genomics, bioinformatics, and AI have enabled significant exploration and optimization of natural products for drug discovery and therapeutic applications. Such innovations overcome some of the challenges associated with traditional drug discovery from natural sources and open up new possibilities in precision medicine and personalized treatments.

I) Genomics and Metagenomics:-

Genomics generally plays a very important role in understanding the genetic makeup of producing organisms. This is because pharmacologically active natural compounds can arise from sequencing medicinal plants, microorganisms, and marine organisms and identify the genes responsible for the biosynthesis of valuable bioactive compounds. Genomics further enables identification of new species as well as exploration of underexploited biological resources. For example, metagenomics - the direct analysis of genetic material from samples taken directly from the environment - has been very crucial in identifying new species of microbes and their potential use in producing antibiotics and therapeutic drugs as part of their production.[126]

Metagenomics also includes the symbionts, such as endophytes, which inhabit inside the plants and produce bioactive compounds. However, microbial communities of these also carry uncharacterized genes that encode new compounds. As such, they represent an exciting new frontier for drug discovery.

II) Bioinformatics:-

Bioinformatics is a tool in processing and analyzing the huge amounts of data generated from genomic studies. It enables scientists to predict the biosynthetic pathways involved in the production of secondary metabolites, thus discovering natural products. Thus, using bioinformatics, scientists are also capable of predicting the structure and function of unknown compounds, speedening up the identification and characterization of natural products.[127]

In addition, through bioinformatic shell, such as antiSMASH, for antibiotics and secondary metabolites, biosynthetic gene clusters responsible for production in microbes are identified. These computational tools of great importance in mining genomes to seek new natural products, that can be synthesized later and tested for therapeutic use.

III) Artificial Intelligence (AI) and Machine Learning:-

Artificial intelligence and machine learning have revolutionized the drug discovery process through speedy assessment of enormous datasets potentially capable of predicting pharmacological properties of natural compounds. AI can help researchers sort through vast libraries of natural products, thereby analyzing their molecular structures and forecasting potential biological activities at high accuracy levels. AI-generated models can also predict drug candidates just by scanning the molecular databases and predicting with a certain accuracy how natural compounds might behave in interacting with biological targets.

AI has turned out to be invaluable for lead optimization if it can predict the efficacy, toxicity, and pharmacokinetics of a compound before it goes into clinical trials. That saves valuable time and money in drug development. For instance, AI has already identified the new antibiotic halicin with a broad spectrum of activity by screening a vast chemical library for predicting the compound's bactericidal properties.

IV) Cheminformatics and Molecular Modeling:-

Cheminformatics and molecular modeling augment AI in natural product research as they provide a computational framework for modeling molecular structures and simulating their interactions with biological targets. Thus, researchers will, to some extent, predict the binding affinities and pharmacological properties of natural compounds before expensive and time-consuming laboratory experiments are conducted in the laboratory. For example, molecular docking studies predict the behavior a natural compound may exhibit toward a protein receptor in relation to its potential therapeutic effects.

For instance, Chiminformatics databases, such as ZINC and PubChem, contain large libraries of small molecules, many of which are natural products, together with data about their bioactivity. This would allow the virtual screening of large chemical libraries, because it may make the discovery of promising drug candidates from natural sources easier.

V) Synthetic Biology and Metabolic Engineering:-

Synthetic biology is also a revolutionary technology which enables the design of organisms that can produce natural compounds with much greater sustainability and scalability. Genetic changes in the metabolic networks of microbes are made to enable scientists to overproduce particularly valuable natural products either challenging or impossible to obtain from their natural sources in sufficient quantities or produced in insufficient quantity. For example, the compound of antimalarial drug artemisinin was first extracted from the Artemisia annua plant and then manufactured by using synthetic biology to engineer yeast so it would biosynthesize the compound.

It is true that metabolic engineering allows researchers to optimize the biosynthetic pathways of microorganisms and plants for higher yields and consistency of natural product production. This approach improves access to crucial drugs while also reducing the environmental damage associated with harvestings of medicinal plants from the wild.

B] Collaboration Between Modern and Traditional Medicine:-

To this end, the integration of traditional medicine with modern healthcare is one of the strategies that have increasingly become a reality towards improving patient outcomes and overcoming global health challenges. The two systems have differing strengths. Traditional medicine has a tendency towards holism or even preventions as opposed to modern medicine, where evidence-based treatments and much more sophisticated technological interventions are relied upon. However, significant barriers separate the two disciplines, including differences in practice, knowledge frameworks, and regulatory standards. Collaboration between the traditional and modern practitioners will be an aspect that would provide all-rounded care, and cultural sensitivity shall be enhanced. Modern health provision can then be delivered optimally within the regions where traditional medicine features predominantly in public health.

I) Bridging Gaps Between Knowledge Systems:-

The biggest challenge, from promoting interaction between traditional and modern medicine, is that of differences between two knowledge systems. Traditional medicine is based on experiences amassing centuries, often orally passed down, but it bears deep imprints of both cultural and spiritual practices. Modern medicine relies on scientific research, clinical trials, and standardized procedures. This will only be filled with mutual respect, open communication, and an understanding of the value that each system contributes to patient care.[88]

There would also be trust and cooperation through programs of mutual exchange between the traditional healers and modern providers. For instance, in China and India where Traditional Chinese Medicine and Ayurveda are an integral part of the health systems, collaborations between practitioners of traditional systems and biomedical professionals have led to more integrated care plans and better results from public health perspectives. This integration not only increased the healthcare reach but also respects and conserved cultural heritage.

II) Integrating Traditional Medicine in Modern Healthcare Systems:-

Other countries have come to realize the incorporation of traditional medicine into their health care sectors as a need in making the service more universal. For instance, the health policies of India and China make provision for the incorporation of traditionally used systems, such as Ayurveda and Traditional Chinese Medicine (TCM), into mainstream healthcare. Such policies aim at encouraging cooperation since practitioners of traditional medicine work together with practitioners of modern medical sciences in hospitals and clinics.

This usually occurs through interdisciplinary teams, where the traditional healers are involved in the treatment of chronic diseases such as diabetes, cancer, and heart conditions. The teams can make complementary approaches that is, the combination of symptomatic treatment by modern medicine with the holistic care and lifestyle guidance provided by the traditional practitioner.[128]

III) Improving Patient Care and Public Health Outcomes:-

Collaboration between traditional and modern health care systems has been proven to improve the care provided to patients, particularly to rural and deprived communities who have very limited access to modern medical facilities. Traditional medicine often plays the role of a first-line care by providing preventive and therapeutic solutions that are culturally familiar and accessible. Involving traditional healers in national health systems ensures that patients get the types of care, which reduce the burden that modern healthcare facilities place upon them and offer a more holistic approach in treating patients.

For example, where traditional healers collaborate with modern healthcare service providers in sub-Saharan Africa, the treatment of malaria has been enhanced, leading to increased compliance and better outcomes for patients. It was the use of Artemisia annua, popularly known as sweet wormwood, for the treatment of fever that formed the basis for the development of artemisinin-based combination therapies whose major emphasis lies in modern antimalarial treatments. Thus, such examples illustrate the potential for using traditional medicine to shape drug discovery in modern medicine and to increase possibilities in therapy.

IV) Challenges and Opportunities for Collaboration:-

Although the opportunities and challenges of interconnecting traditional and modern health systems are profound, there are still many problems related to effective collaboration. One very significant issue is the lack of standardization and regulation within traditional medicine. Variations in diagnostic approaches, treatment procedures, and definitions of health and disease make it complicated to create a coherent framework for integration. However, modern healthcare providers might also distrust the appropriate application of traditional treatments as their effectiveness and safety are not scientifically verified and they do not carry out strict clinical trials.

There is, therefore a sound rationale for cross-disciplinary training programs, and there should be promotion of collaborative research initiatives that would help establish scientific validation for traditional practices so that safety and efficacy can be ensured regarding the remedies in use. There is also the need to have regulatory frameworks drawn out for standardizing the practice of traditional medicine so that it becomes well-integrated into the mainstream in terms of modern healthcare delivery.

10. Conclusion :-

i) Natural products and traditional medicine are very important for modern health care, a source of great resource that can add something worthwhile to drug discovery, preventive care and chronic disease management.

ii) The ancient systems of practices, like Ayurveda, Traditional Chinese Medicine (TCM), and Indigenous practices, continue to provide the holistic approach to health and wellness throughout the ages, and integration of these ancient approaches into modern medical frameworks continues to receive global recognition.

iii) Bioactive compounds of both plants, marine organisms, animals, and microorganisms have been sources for the formation of many drugs nowadays, for example, paclitaxel, penicillin, and artemisinin.

iv) More recently, genomics, bioinformatics, and AI/ machine learning are speeding up the discovery and optimization of natural products, showcasing them for personalized medicine and treatment of complex diseases.

v) While issues like standardization, safety concerns and ethics component, including biopiracy, are there, integration of traditional users with modern users is necessary to harmonize the two.

vi) Organizations like the WHO are efforts that, on the basis of international acceptance of traditional medicine, encourage nations to adopt these practices as a part of an integrated health care system.

vii) Going forward, additional research, regulation, and technological innovation will eventually unlock the full potential for natural products and traditional medicine for improvement of health outcomes worldwide.

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