IMPACT OF COUNTERFEIT MEDICINES

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***Abstract*: Pharmaceutical Counterfeiting and purchasing of medicines from illegal distribution have become more common concerns worldwide. The counterfeit medicines are causing a major impact on public health and on the pharmaceutical business across the globe. Counterfeiting involves networks of manufacture and distribution that have become an integral part of crime. Specific measures are getting implemented by the WHO to combat the falsified drugs and overcome the problems caused by them. Although the practice of counterfeiting is not likely to ever disappear, it should be controlled by the governments and can be overcome if all the relevant parties combine forces to identify and disrupt this counterfeit chain.**

***Keywords:* Counterfeit, public health, pharmaceutical business, combat, falsified drug.**

● Introduction:-

Counterfeiting in pharmaceutical products is an increasing worldwide dilemma with a profound impact on lower income countries (LIC) and lower middle-income countries (LMIC). It's also becoming a problem in high-income countries (HIC).There is no clear, agreed international definition of counterfeit medicines[1].The term counterfeit drug has been defined differently in numerous countries limiting both the exchange of knowledge between countries and a true understanding of the extent of the matter globally[8].The most widely used definition within the literature, within the last 20 years, is that given in 1992 by the WHO. This defines a counterfeit medicine as a drug which is deliberately and fraudulently mislabelled with regard to identity and/or source. Counterfeiting can apply to branded and generic products[1].Substandard, spurious, falsely labelled, falsified and counterfeit (SSFFC) medical products are called Counterfeit Medicines[7].

It is believed that up to 10% of all medicines sold worldwide are counterfeit, with higher prevalence in regions where drug regulatory and enforcement systems are weakest[2].One of the foremost complex and challenging problems faced as a results of the worldization of health-care delivery is securing the integrity and safety of the global medicines supply chain[3].Counterfeiting can apply to both branded pharmaceuticals and their less costly generic counterparts.In fact, generic drugs are sometimes confused with counterfeit medications, which can pose an obstacle to the widespread use and acceptance of generic medications[4].Counterfeit drugs are a serious explanation for morbidity, mortality, and loss of public confidence in medicines and health structures[5].Counterfeit and falsified drugs can have a heavy impact upon human health[6].

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These drugs can also influence microbial resistance as well as have an effect on pharmaceutical companies' profits and branding. In 2017, WHO analysed drug samples and found that 10.5 percent of pharmaceutical drugs in low and middle-income countries are fake or substandard.Many south-east Asian countries like China and India are developing nations so may have counterfeit drugs at these levels[6].Counterfeit products are those: 1) without active pharmaceutical ingredients (APIs), including the wrong ingredients,which may or may not be toxic. 2) with incorrect quantities of these APIs. 3) with fake or counterfeit packaging[8].The most common substandard/counterfeit antimicrobials include beta-lactams (among antibiotics) and chloroquine and artemisinin derivatives (among antimalarials).The most common type of substandard/counterfeit antimicrobial drugs have a reduced amount of the active drug, and the majority of them are manufactured in Southeast Asia and Africa[9].It appears that most counterfeits are produced in Asia and brought into patient homes from purchases made while abroad and from internet pharmacies. Practitioners should be vigilant regarding very minor changes in drug appearance or effectiveness and not automatically assume treatment failures are due to a lack of compliance [10].Official government agencies, international bodies, and academia in Asian and African countries have always been aware of the availability of counterfeit pharmaceuticals. However, the data on counterfeit pharmaceuticals in India is only made available through the official government source[15].

- **Effect of Counterfeit Medicine:-**

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Counterfeit medicines pose a significant threat to public health. Up to fifteen you look after all drugs sold worldwide are estimated to be fake. Fake medicines are found everywhere within the world[13].Counterfeit drugs have variety of adverse effects on both health and economic aspects of a population[11].Bad quality counterfeit medicines can affect individuals in an exceedingly type of ways such as:-

- Adverse effects (for example toxicity) from incorrect active ingredients.
- Failure to cure or prevent future disease, thereby increasing mortality, morbidity and also the prevalence of disease.
- Contributing to the progression of antimicrobial resistance and drug-resistant infections.
- A loss of confidence in health care professionals, health programmes and health systems.
- Increasing out-of-pocket and health system spending on health care.
- Lost income because of prolonged illness or death.
- Lost productivity costs to patients and households when seeking additional medical aid, the results of which are felt by businesses and also the wider economy.[12]

At the larger scale of community, national or international public health, counterfeit drugs can have devastating effects by contributing to the event of antimicrobial resistance[14]. Recently the US Trade Representative has placed India and 12 other countries on the 'Priority Watch List'. They allege 20% of medication within the Indian market to be counterfeit drugs because of India's poor history of protecting material possession Rights (IPR)[11]. Ingestion of counterfeit drugs may end up in damage to the liver, kidneys,heart and therefore the central systema nervosum [13]. There are various scenarios where counterfeit drugs can have adverse effects on health like the counterfeit drug has the incorrect active ingredient. This scenario would be to appreciate the patient taking another drug rather than the prescribed without knowing it[11]. because of incorrect ingredients where the results may vary from being unexpected (eg:when cotrimoxazole contains diazepam) to cause hypersensitive reactions (eg: artesunate tablets containing chloramphenicol). Additionally, it can't be assumed that counterfeit products containing APIs are going to be subtherapeutic, as in some cases,they contain over the stated amount and for those drugs with narrow therapeutic indices, this increases the potential for adverse effects[8].

- **How to differentiate genuine and fake drug:-**

Substandard drugs may be detected by different methods, including inspection, colorimetric methods, chromatography, and spectrometry[9].Consumers and authorities are finding it increasingly difficult to spot illicit versions of medication through visual inspection alone. Despite the legitimate pharmaceutical industry consistently implementing new measures to assist to guard genuine products and permit for easier distinction from counterfeit products,14 criminals are ready to quickly adapt to those modifications with the assistance of rapidly enhancing technology.4 As shown in figure below technological advances have greatly enhanced counterfeiters' ability to make packaging that's exceptionally near the drugs authentic packaging. Criminals are getting increasingly ready to mimic logos using colour shifting inks and holographs. Tools, including 3D printers, are getting progressively more common as a production method for components of, or entire packaging[7].

Figure:-Counterfeit packaging recovered during Operation Zambezi in 2009 [7].

A three-level approach consisting of various internal control procedures has been proposed to detect substandard/counterfeit drugs. Level 1 includes inspection to work out the standard of packaging and labeling. Level 2 encompasses methods which will exhaust the sector. Level 3 requires the equipment of a longtime laboratory to see drug quality in step with established specifications. New technologies like spectroscopy , X-ray methods , data matrix type, oftenness identification (RFID) labels, holograms, engraving, invisible prints, and nanotechnologies have increasingly been accustomed determine quality of antimicrobials and should help increase the efficacy of detection of substandard/counterfeit antimicrobials. However, such solutions are expensive and infrequently available only to higher-income countries. Thus, since technology may improve the detection of low-quality drugs, it'd be important that these methods also will be available in developing countries, where counterfeit products are the foremost common[9]. Many anti counterfeiting technologies are being utilized by pharmaceutical companies to make sure distribution of the authentic product from the manufacturing site to the pharmacy. Among these technologies employed by pharmaceutical manufacturers are holograms, color-shifting inks, and embedded codes, images, and dyes. These anti counterfeiting features allow pharmacists to spot suspicious medications as possible counterfeits[4].

1)Barcodes:- India is attending to make barcoding on pharmaceutical products mandatory to create drugs traceable and reduce counterfeits. A report by the Office of the US Trade Representative (USTR) found India to be the most important producer of counterfeit drugs within the world[6].

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When drugs are scanned, they'll immediately be identified. This improves the traceability of medicines, allowing fakes to be easily identifiable[6].

A number of strategies are applicable to fighting this problem.

2) RFID:- Radio-frequency identification (RFID) chips are used inside the cap or under the label on bottles of pharmaceutical products. These RFID chips are also programmed with the batch number or another identifying letters or numbers in order that when the bottle is scanned, one may tell whether it's genuine or not. Another technology that has been used successfully in other industries is to laser etch a batch number, serial number or another identifying number on the glass or plastic container beneath the label on the bottle itself. If there's any question concerning possible inactivity, it's easy to appear under the label to determine whether there's an etched number that's correct for that product, batch and expiration date[10].

[16].

Figure:-RFID CHIP.

3)Holograms:- Holographic technologies provide a simplified means for consumers to spot the authenticity of a drug. The advantage of hologram is that they'll be applied at the item
level, like a bubble pack or vials.Holograms themselves can even be eventually duplicated by counterfeiters, making the initial investment by the brand owner ineffective. Holograms also
do not provide the brand owner with an implementable protocol for supply chain management, track-and-trace ability (e-pedigree), or with the intelligence that's required within the event that counterfeiting occurs. Other more technologically sophisticated measures include nano-tagging or chemical/physical forensic measures. These are much more expensive and haven't yet been employed by the pharmaceutical industry to an appreciable extent[14].

Figure:- TWO BLISTER PACKAGES OF THESE ANTIMALARIAL DRUGS, ARTESUNATE,ONE GENUINE (RIGHT), AND ONE COUNTERFEIT (LEFT). A WELL-CRAFTED HOLOGRAM IS THE ONLY DISTINGUISHING FEATURE OF GENUINE PRODUCT[16].

4) Mobile verification:- There's unique code for every product which may be verified by sending texts to the amount given. Manufacturer Sprint these codes on packaging, and monitoring begins the minute the merchandise leaves the factory. This manner of consignment is protected while in transit until they reach their destination[14].

5)Mass Encryption Technology:- During this technology, every product is given a novel digital identity that's generated by a computer based encryption engine. the identical software is in a position to decrypt the digital code. The encrypted code itself is typically a 16-digit alphanumeric code which will be displayed in:

Figure:- A linear format—Scripted format----HJ21WFOHU20KB8N72-D Data Matrix barcode--

Figure:- 2-D barcodes, which are now becoming the industry standard, are printed on packaging during manufacture and therefore provide each medicine with the identity before it enters the supply chain[16].

- **Economy wide effect of counterfeit medicine:-**

Counterfeit medicines may additionally end in higher health care costs, as patients may require additional treatment to accommodate potential adverse effects of ineffective or damaging drugs. Physicians and health care providers rarely suspect counterfeit or substandard drugs because the reason for a patient's poor therapeutic response. Accordingly, they most often respond by ordering more tests or repeating the course of treatment (OECD, 2016).In addition to the direct effects on consumers, producers and governments, counterfeits can have broader, economy-wide effects in an exceedingly number of areas, including on the environment, foreign investment and crime. There may additionally be impacts on economic performance; EUIPO (2019) reports that counterfeits lead to an estimated EUR 16.5 billion of lost sales and affect quite 80 000 jobs within the pharmaceuticals sector and other sectors that sell goods and services to it[12].Counterfeit drugs cause economic burden by causing a subsequent increase in morbidity, adverse drug reactions and drug resistance. additionally to increased morbidity there's an increased mortality, which might also result in loss of economic potential. Sale of counterfeit drugs will harm sale of genuine drugs hence, affecting companies that have invested in quality, research and development of medication. This might also deter companies from investing in research and development further as deter foreign investments. there's also a major loss of government income to the government. additionally to the current large amounts must be spent to safeguard the provision chain of medication and creation of systems that may detect counterfeit drugs[11].The impact of counterfeits on legitimate producers are multiple, including lost sales, costs of protecting brands, loss of reputation, the potential cost of managing the disposal of counterfeits and litigation costs involving counterfeiters and possibly people that were unknowingly victimised by counterfeits[12]. Many pharmaceutical companies lose large amounts of cash because their products are being counterfeited and sold at cheaper rates. Drug therapy has financial implications both on the individual and therefore the economy. When the incorrect drug or counterfeit is employed it's waste and when excess or under dose of the correct drug is employed, it's also wasteful. It affects the individual finances because there's an increased cost of therapy. Man hours also are lost to illnesses that may have resolved much earlier if the correct drugs were taken[13].

- **Role of pharmacist in preventing counterfeiting of medicine:-**

Pharmacists are vital in ensuring the protection of medicines utilized by patients. Furthermore, they're answerable for the integrity of the availability chain, starting from manufacturer to distributor and, ultimately, to the patient. Specifics on how pharmacists, pharmacy students, and technicians can combat counterfeit medications are shown in TABLE below[4].

Table 1. Role of Pharmacists in Preventing Distribution of Counterfeit Medications

Ensure purchase of medications from known, reliable sources
Warn patients about the dangers of purchasing medications over the Internet
Beware of fraudulent distributors
Monitor counterfeit product alerts
Inspect all medication packages for faulty seals and labels
Report any suspicious counterfeit medications through MedWatch
Educate pharmacy students, technicians, and other pharmacists about the risks

Source: References 1, 11.

[4].

The pharmacist should follow all the above measures to prevent counterfeiting of medicines.

- **Measures to prevent Counterfeiting of medicines:-**

It is time the medical fraternity takes a stand against dispensing of loose drugs by physicians and pharmacists alike. The loose drugs don't mention the name of the drug, its manufacturer, neither the date of manufacture nor the date of expiry. The manufacturers also are more likely to stick to quality standards just in case the drugs bear their name. the standard of loose drugs is additionally more susceptible to deterioration in improper conditions. This step could also reduce the danger of dispensing a wrong drug. The dispensing of labeled drugs would also reduce the doctor-patient asymmetry, because the patients would become attentive to their prescriptions. Currently some practitioners give loose drugs to their patients and also the patients are unaware of the drugs that they're consuming. there's an argument that strip packing results in 'Quality Drugs' which the proper to 'Quality Drugs' an important a part of Right to Life.Except for some states most state pharmacies which cater to government institutions are buying drugs in strip packing and this can be a decent sign.The maintenance of the drug quality is a vital component of medical aid.There is a recommendation to impose executing to those that produce or sell counterfeit drugs in India, on quote a previous central health minister, "Profiting from spurious drugs which may harm or kill innocent people is comparable to execution." This slaying is unfortunately perpetuated from within the country, is the maximum amount a threat to its citizens as a act of terrorism, and will unite all concerned to counter the scourge[5].Whenever counterfeit products are seized they must be examined from a forensic intelligence perspective, with all data obtained being stored into a database which is able to help enforcement tackle illicit manufacture and trafficking of those items. The chemical profile should be mapped together with a general physical examination of the medication and packaging. Batch numbers, best before dates and the other relevant information should be entered which, after time, will give quick searching of seized products against known counterfeit batches. This information could further be mapped to produce statistics on the assembly and distribution within the network and permit calculated attempts to dismantle the matter from the source to be made[7].

Groups working together may help to combat matters. These measures mean that the impacts will hopefully be reduced, improving human health and decreasing the prices for pharmaceutical companies[6].We also believe identification of specific public health–sensitive counterfeit drug categories for policymaking attention and priority setting should be used. for instance, the general public health consequences related to counterfeit vaccines should be a priority in counterfeit drug surveillance.It should even be noted that middle-income countries are critical in focusing efforts to push global drug safety. Although better data are clearly necessary, per a range of measures—economic, geographic, and third-party Counterfeit Incident reporting—Middle Income countries appear to possess the potential for greater counterfeit medicines production and penetration in their legitimate supply chain[3].Another strategy that holds promise would be to register and control the sale of tablet presses and capsule-filling machines, moreover because the excipients that are employed in tablet and capsule manufacture. during this way, it'd be possible to stay track of the owners of such equipment and therefore the location of apparatus capable of producing pharmaceutical tablets and capsules. We see something similar with the restricted over-the-counter (nonprescription) sales of ephedrine-containing decongestants, since ephedrine could also be accustomed to manufacture methamphetamine[10].Countries must close to deal with the problem of counterfeit drugs and agree on one definition. there's a desire to conduct reliable unbiased studies on the prevalence of counterfeit drugs in World, which might help in improvement of the healthcare system[11].It is not really possible to totally eradicate pharmaceutical counterfeiting, but it's possible to create the longer term production, shipping, smuggling and distribution of those products so complex, difficult, time consuming and expensive that the perpetrators may elect to search out an easier area for his or her future exploits across the globe[10].

- **Conclusion:-**

Drugs play an important role in quality of life. In some regions of the globe, the trafficking of counterfeit medicines are crimes of opportunism, and in others, part of a fancy and arranged global criminal enterprise. Effectively addressing it must combine both enforcement and public health perspectives further as public and personal resources, for no single entity can accomplish this goal alone.Counterfeit medications is also detrimental to a patient's health status. the utilization of counterfeit drugs may end in adverse side effects, treatment failure, resistance, toxicity, and even death. Counterfeit medicine poses a heavy threat to public health and has taken a silent devastating toll on humanity because of the dearth of reporting in some critically affected areas. Additionally to past and present losses thanks to fake drugs, the long run of world health is in danger. Disease causing agents can develop resistance to genuine drugs.It is important that pharmaceutical companies, healthcare professionals, pharmacists, and patients be educated about counterfeit medications and therefore the laws being enforced to stop this crime. the employment of proper anti counterfeiting devices should be exhausted in order to combat this problem of falsified medicines. Government should take serious measures to conclude this major threat. The pharmaceutical industries should develop more advanced technologies by which the merchandise can't be counterfeited. and Therefore the public should be educated about the difference between the fake and genuine drugs.

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