Substandard medicines CDSCO

Curated by Pragya Chaudhari (S.Y.B. Pharm) Guided by Dr Shilpa Chaudhari

Substandard medicines could be three times more prevalent than what the reports show according to two new studies. These data have serious implications on health in a country where 58.2% of the total health expenditure is an out-of-pocket cost burden on people, according to the World Health Organization, and where medicines alone account for between 70% and 77% of health spending. Substandard drugs work less effectively, causing disease to run a longer course, and can even require a new prescription during treatment. Substandard drugs also contribute to antibacterial resistance, a threat that has doubled in the last five years in India, as reported earlier. About 4.5% of the drugs in the Indian market are substandard, according to surveys by the Central Drug Standard Control Organisation (CDSCO), the official regulatory authority. Reputed brands too fail to meet quality standards. Experts believe that more lucrative routinely prescribed drugs are at higher risk of failing quality standards, as this new study, published in the December 2015 Journal of Applied Pharmaceutical Science, concluded, after testing 32 samples of diclofenac sodium, a popular pain killer. A second study, published in the International Journal of Pharmacy and Pharmaceutical Sciences, evaluated 46 samples of amoxicillin trihydrate, a fast-moving antibiotic.

Studies showed that substandard medicine incidences of 15.62% for diclofenac sodium and 13.04% for amoxicillin trihydrate, were reported, even some higher-priced medicines from reputed sellers failed to measure up.

To make the grade, a tablet must contain between 90% and 110% of the active ingredient named on the label, according to the Indian Pharmacopoeia Commission, an autonomous Indian health ministry institution. However, the CDSCO offers a 5% grace margin on that lower limit.

Government surveys reveal a falling incidence of substandard and spurious drugs in the Indian market—from about 9% in the mid-1990s, to 4.5% in recent years (2015 Indian Journal of Pharmaceutical Sciences)

Spurious medicines alone, distinguishable from substandard products for being imitations of (usually) popular branded drugs, with ingredients that may or may not match their label, make up a negligible part of the Indian drug market as per the CDSCO—0.046% according to its 2009 Report on Countrywide Survey for Spurious Drugs and 0.11%, according to last year's regular sampling. Last year, the CDSCO tested 74,199 samples across the country, a 150% increase in sample size over 2012.

However, that is still a drop in the ocean for the world's third-largest pharmaceutical market by volume India consumes 383 billion medicines per annum, according to this 2015 report, but

details of the manufacturing units producing those tablets are virtually unavailable.

CDSCO Sample Study Results

YearTested	Samples	Substandard	Spurious/Adulterated	% Failed
2011-12	48,082.00	2,186.00	133.00	4.82
2012-13	58,537.00	2,362.00	70.00	4.15
2013-14	72,712.00	3,028.00	118.00	4.32
2014-15	74,199.00	3,702.00	83.00	5.10

CDSCO: Central Drug Standard Control Organisation, Source: 1. Lok Sabha 2. Press Information Bureau

What happens to drugs that fail quality standards?

Manufacturers of drug samples that fail CDSCO tests for ingredients, dissolution, sterility, toxicity, among others, are served notice. In case of failure to correct the processes or repeated instances of non-compliance, the manufacturer's product licence is suspended and in extremely rare circumstances, even cancelled. However, in case a given manufacturer has multiple production lines, then a short-term suspension of a single production licence may not prove to be an effective deterrent. Partial suspension of manufacturing by a company with unscrupulous intentions also may not comfort consumers.

Conclusion (Pragya Chaudhari)

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A faster and cheaper way to produce new antibiotics by University of Bristol

Curated by Pragya Gigoo (S.Y.B. Pharm) Guided by Mr Vaibhav Vaidya

A novel way of synthesizing a promising new antibiotic has been identified by scientists at the University of Bristol.

By expressing the genes involved in the production of pleuromutilin in a different type of fungus, the researchers were able to increase production by more than 2,000 per cent.

With resistance growing to existing antibiotics, there is a vital and urgent need for the discovery and development of new antibiotics that are cost effective. Promising developments are derivatives of the antibiotic pleuromutilin, which are isolated from the mushroom Clitopilus passeckerianus.

These new compounds are some of the only new class of antibiotics to join the market recently as human therapeutics. Furthermore, with their novel mode of action and lack of cross-resistance, pleuromutilins and their derivatives represent a class with further great potential, particularly for treating resistant strains such as methicillin-resistant Staphylococcus aureus (MRSA) and extensively drug resistant tuberculosis (XTB).

However, mushrooms are basidiomycete fungi which are not generally amenable to strain improvement and fermentation.

Therefore, in collaboration with pharmaceutical company GSK, Bristol scientists carried out research to identify the genes involved in the production of pleuromutilin. They discovered that a seven-gene cluster is required to produce the antibiotic in C. passeckerianus.

The seven-gene pleuromutilin cluster was then reconstructed within a more industrial fungus, Aspergillus oryzae which belongs to a different group of fungi, the ascomycetes. This resulted in a significant increase (2,106 per cent) in production.

This is the first gene cluster from a basidiomycete to be successfully expressed in an ascomycete, and paves the way for the exploitation of a metabolically rich but traditionally overlooked group of fungi.

Co-author of the research, Professor Gary Foster said: "This was a massive team effort over many years to achieve this major breakthrough. It involved, in the School of Biological Sciences, the drug discovery team led by myself and Dr Andy Bailey, with Dr Colin Lazarus on alternative expression platforms. In addition, significant effort came from chemists at the University of Bristol led by Professor Chris Willis and Professor Russell Cox, and collaborative scientists in GSK. "With this development, we are now ideally placed to develop novel derivatives and new antibiotics and produce them rapidly and cost effectively – something which is desperately needed globally.

" A novel semisynthetic pleuromutilin, retapamulin, was launched by GSK as the drug Altabax.

Conclusion (Pragya Gigoo)

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Conclusion (Vaibhav Vaidya)

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Atrial Fibrillation risk higher in depressed people

GENETIC ENGINEERING AND BIOTECHNOLOGY NEWS

Curated By- Raju Mane (S.Y. B Pharm) Guided by Ashish Kulkarni

Depressed people have an increased risk of atrial fibrillation, according to a study ("Depression, antidepressants, and the risk of non-valvular atrial fibrillation: A nationwide Danish matched cohort study") published in the *European Journal of Preventive Cardiology.* Medication was not responsible for the high frequency of atrial fibrillation in depressed people, stressed the researchers.

"It is common knowledge that there is a connection between the mind and the heart. Depression predicts the development of coronary artery disease and worsens its prognosis. Our study investigated whether depression is also linked with atrial fibrillation," says study author Morten Fenger-Grøn, senior statistician, research unit for general practice, Aarhus University, Denmark. Atrial fibrillation is the most common heart arrhythmia. It causes 20–30% of all strokes and increases the risk of dying prematurely. Previous studies have found associations between depression and both more severe symptoms and higher mortality in atrial fibrillation patients. Antidepressants have been linked with some serious, but rare, heart rhythm disturbances, prompting the question of whether they might also raise the risk of atrial fibrillation. This study investigated the association of depression, and antidepressant treatment, with the risk of developing atrial fibrillation. Filling a prescription for antidepressants for the first time was used as an indicator of depression. "Depression is associated with an increased risk of a series of cardiovascular diseases and with increased symptom burden in patients with atrial fibrillation. The aim of this study was to determine the association between depression as well as antidepressant treatment and the risk of incident atrial fibrillation. "A nationwide register-based study comparing the atrial fibrillation risk in all Danes initiating antidepressant treatment from 2000 to 2013 (N¼785,254) with that in a 1:5-matched sample from the general population.

"Cox regression was used to estimate adjusted hazard ratios (aHRs) and associated 95% confidence intervals (95% CIs), both after initiation of treatment and in the month before when patients were assumed to have medically untreated depression.

"Antidepressant treatment was associated with a three-fold higher risk of atrial fibrillation during the first month (aHR¼3.18 (95% CI: 2.98–3.39)). This association gradually attenuated over the following year (aHR¼1.37 (95% CI: 1.31–1.44) 2–6 months after antidepressant therapy initiation, and aHR¼1.11 (95% CI: 1.06–1.16) 6–12 months after). However, the associated atrial fibrillation risk was even higher in the month before starting antidepressant treatment (aHR¼7.65 (95% CI: 7.05–8.30) from 30 to 15 days before, and aHR¼4.29 (95% CI: 3.94–4.67) the last 15 days before).

Overall, 0.4% of patients were diagnosed with atrial fibrillation from 30 days before to 30 days after antidepressant treatment.

“Antidepressant users had a substantially increased atrial fibrillation risk, particularly before treatment initiation. Whether this mirrors a causal relation between depression and atrial fibrillation may have large consequences for public health and should be discussed.”

“Filling a prescription for antidepressants, which we used as an indicator of depression, was associated with a three-fold greater risk of atrial fibrillation. The decrease with time could suggest that treatment may alleviate this risk,” said Fenger-Grøn.

The risk of atrial fibrillation risk was even higher in the month before starting antidepressants. “This suggests that antidepressant medication itself is not associated with the development of atrial fibrillation,” he continues. “If you are depressed, there is no reason to worry that taking drug treatment will cause atrial fibrillation.”

Conclusion (Raju Mane)

Effect of depression and the antidepressant treatment, results found were shocking suggesting that people suffering with atrial fibrillation before treatment developed depression as a symptom that was the indicator of development of the atrial fibrillation. But with the treatment the danger of atrial fibrillation was found to be decreased. So the antidepressant treatment was found to be a preventative measure in countering atrial
fibrillation.

Conclusion (Ashish Kulkarni)

This study investigated the association of depression, and antidepressant treatment, with the risk of developing atrial fibrillation. The aim of this study was to determine the association between depression as well as antidepressant treatment and the risk of incident atrial fibrillation. Antidepressant treatment was associated with a three-fold higher risk of atrial fibrillation during the first month

Roche's supplemental biologics Biospectrum news

Curated By Pournima Singh S Y B Pharm Guided by Dr Pallavi Chaudhari

Roche SIX: RO, ROG; OTCQX: RHHBY) announced that the US Food and Drug Administration (FDA) has accepted the company's supplemental Biologics License Application (sBLA) for Tecentriq® (atezolizumab) in combination with Abraxane® [albumin-bound paclitaxel; nab-paclitaxel]) and carboplatin for the initial (first-line) treatment of people with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR or ALK genomic tumour aberrations.

Lung cancer is a challenging disease to treat, and this review takes us one step closer towards offering a new treatment option that has shown a clinically meaningful survival benefit in the treatment of this type of disease.

The FDA recently approved Tecentriq in combination with Avastin, paclitaxel and carboplatin (chemotherapy) for the initial treatment of people with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumour aberrations. Tecentriq is also approved by the FDA to treat people with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy.

The co-primary endpoints were:

- PFS as determined by the investigator using RECIST v1.1 in people without EGFR or ALK mutations, assessed in the ITT-WT population
- OS in the ITT-WT population

The IMpower130 study met its OS and PFS co-primary endpoints as per the study protocol. The interim analysis showed that Tecentriq plus chemotherapy helped people live significantly longer compared with chemotherapy alone (median OS=18.6 versus 13.9 months; hazard ratio [HR]=0.79; 95% CI: 0.64–0.98; p=0.033) in the intention-to-treat wild-type (ITT-WT) population.

Conclusion (**Pournima Singh**)

Roche announced that the US Food and Drug Administration FDA) has accepted the company's supplemental Biologics License Application sBLA) for Tecentriq atezolizumab)in combination with Abraxane and carboplatin for the initial first-line treatment of people with metastatic non-squamous non-small cell lung cancer NSCLC) who do not have EGFR or ALK genomic tumour aberrations. Lung cancer is a challenging disease to treat, and this review takes us one step closer towards offering a new treatment option that has shown a clinically meaningful survival benefit in the treatment of this type of disease.The FDA recently approved Tecentriq in combination with Avastin, paclitaxel and carboplatin chemotherapy) for the initial treatment of people with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumour aberrations.

Tecentriq is also approved by the FDA to treat people with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy.The co-primary endpoints were: PFS as determined by the investigator using RECIST v1.1 in people without EGFR or ALK mutations, assessed in the ITT-WT population OS in the ITT-WT population The IMpower130 study met its OS and PFS co-primary endpoints as per the study protocol.

Conclusion (Dr Pallavi Chaudhari)

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No kidding: Donkey's milk is the new elixir By Madhvi Sally ET Bureau Curated by Ashish Kulkarni

Cleopatra used to bathe in it to preserve her legendary beauty, and now more than 2000 years later donkey milk is back in fashion not just as a beauty product but as a super food as well, already fetching Rs 700 for 100 ml. Select entrepreneurs across the country, from Kochi to Pune to Delhi-NCR, have woken up to the ancient wisdom of donkey milk's nutraceutical & therapeutic properties that include anti-ageing and antioxidant qualities to roll out personal care products such as fairness creams, soaps and shampoos besides liquid donkey milk

"There is so much interest and demand, now that consumers are going back to the traditional methods of what their ancestors did to cure them of diseases," said Aby

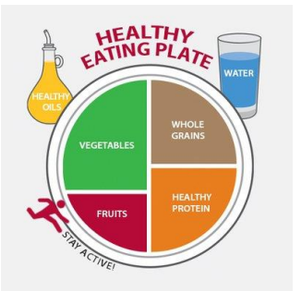
Baby, founder of Dolphin IBA that sells premium beauty products made of donkey milk. "Donkey milk has superior qualities. It is very good for infants, especially those with gastric problems, and for people suffering with skin allergies."

'Donkey's milk is similar to a human mother's milk, and rich in vitamins and essential fatty acids, they said. It has less fat than cow milk. According to the UN's Food and Agriculture Organisation, donkey milk has "particular nutritional benefits". It's seen as an alternative for infants affected by cow milk protein allergies. 'It is in the eligible milk list of many countries including USA, but not yet in India. Here it is largely being used in the cosmetics industry and in a small way in the liquid milk category.

'The government is working to formalise donkey milk business in the country, a senior agriculture ministry official said. "We have suggested Indian Council of Agricultural Research to explore possibilities of promoting donkey milk in India," said Tarun Shridhar, secretary at the animal husbandry department. "It has challenges such as low milk yield and limited shelf life besides developing Taste and market for this new dairy product." 'Once Indian regulators approve it, donkey milk is likely to see a huge growth in the country, industry insiders said.

Conclusion

Donkey's milk has long been used as a preservative of beauty, and now again donkey milk is back in fashion not just as a beauty product but as a super food as well, already fetching Rs 700 for 100 ml.



FDA Updates Nutrition Facts Label USFDA

Curated By- Mukesh Mohite

FDA has published its Final Rule on changes to the Nutrition Facts panel, effective July 26. The changes include listing of added sugars, declaration of vitamin D and potassium and updated daily values for certain nutrients like sodium and dietary fiber, among others. The new Nutrition Facts label will include the following:

An updated design to highlight “calories” and “servings.”

Requirements for serving sizes that more closely reflect the amounts of food that people currently eat. What and how much people eat and drink has changed since the last serving size requirements were published in 1993. By law, the Nutrition Labeling and Education Act, requires that serving sizes be based on what people actually eat.

Declaration of grams and a percent daily value (%DV) for “added sugars” to help consumers know how much sugar has been added to the product. It is difficult to meet nutrient needs while staying within calorie limits if you consume more than 10% of your total daily calories from added sugars, and this is consistent with the scientific evidence supporting the 2015-2020 Dietary Guidelines for Americans.

“Dual column” labels to indicate both “per serving” and “per package” calorie and nutrition information for certain multi-serving food products that could be consumed in one sitting or multiple sittings. Examples include a pint of ice cream and a 3-ounce bag of chips. With dual-column labels available, people will be able to understand how many calories and nutrients they are getting if they eat or drink the entire package/unit at one time.

For packages that are between one and two servings, such as a 20-ounce soda, the calories and other nutrients will be required to be labeled as one serving because people typically consume it in one sitting.

Updated daily values for nutrients like sodium, dietary fiber and vitamin D, consistent with Institute of Medicine recommendations and the 2015-2020 Dietary Guidelines for Americans. Daily values are reference amounts of nutrients to consume or not to exceed and are used to calculate the %DV that manufacturers include on the label.

Declaration of vitamin D and potassium that will include the actual gram amount, in addition to the %DV. These are nutrients that some people are not getting enough of, which puts them at higher risk for chronic disease. The %DV for calcium and iron will continue to be required, along

with the actual gram amount. Vitamins A and C will no longer be required because deficiencies of these vitamins are rare, but these nutrients can be included on a voluntary basis.

“Calories from Fat” will be removed because research shows the type of fat is more important than the amount. “Total Fat,” “Saturated Fat,” and “Trans Fat” will continue to be required. An abbreviated footnote to better explain the %DV. The FDA is also making minor changes to the Supplement Facts label found on dietary supplements to make it consistent with the Nutrition Facts label.

Most food manufacturers will be required to use the new label. Manufacturers with less than $10 million in annual food sales will have an additional year to comply with the new rules. The FDA plans to conduct outreach and education efforts on the new requirements.

The iconic Nutrition Facts label was introduced more than 20 years ago to help consumers make informed food choices and maintain healthy dietary practices. In March 2014, the FDA proposed two rules to update the label, and in July 2015, issued a supplemental proposed rule. The Nutrition Facts label regulations apply to packaged foods except certain meat, poultry and processed egg products, which are regulated by the U.S. Department of Agriculture’s Food Safety and Inspection Service.

The Academy of Nutrition and Dietetics and its member registered dietitian nutritionists analyzed the changes and welcomed the changes. “We applaud the FDA and are thrilled that the new Panel largely aligns with recommendations the Academy submitted to the FDA to help everyone make more informed and nutritious decisions when choosing foods to fit their lifestyles and needs,” said registered dietitian nutritionist and Academy Spokesperson Lori Zanini. “The new Panel better reflects serving size, nutrients and ingredients that people should focus on, and it updates current percent of Daily Values.”

Conclusion

The new Nutrition Facts label will include an updated design to highlight calories and servings. Requirements for serving sizes that more closely reflect the amounts of food that people currently eat.