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NEWSLETTER

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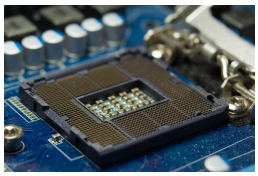
Exben Pharma & Chemical Benchmarking

WHAT'S COMING OUR WAY IN HEALTHCARE?

"Downstream" of the Human Cell Atlas project (see last newsletter), here we look at what is /maybe coming, somewhat sooner, to influence human health.

JUST A THOUGHT: "Medical Devices" range from leeches & maggots to brain implants eg "Neurolink"



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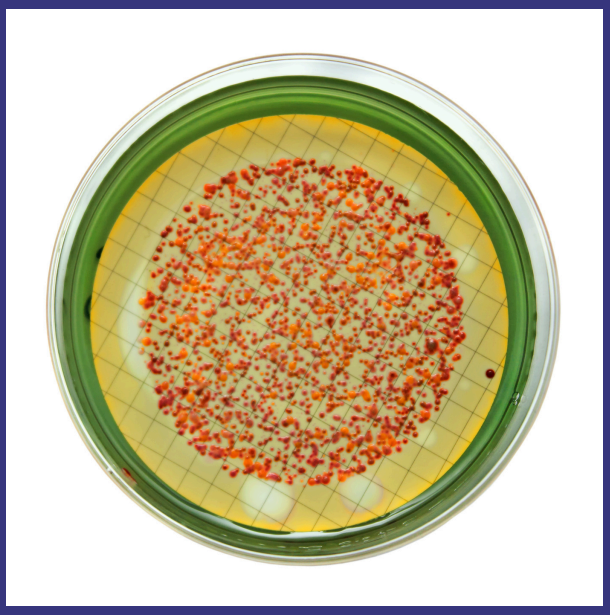
New antibiotics against the "Super Bugs"?

By Steve Biddulph
Fellow of Royal Institute of Microbiology. Board level pharma experience. QSM and Aseptic Manufacturing & Control Expertise

Many species of bacteria cause infections that are proving very difficult to cure are major cause of concern to the medical profession. This is due to the overuse of antibiotics, increasing bacterial resistance and, somewhat strangely, under prescribing antibiotics (that allows residual populations to survive in low numbers in patients).

The search for effective remedies has proved difficult against such organisms as Cl. difficile, S. aureus, Ps. areuginosa, Ps. cepacia, several species of Streptococci and Acinetobacter. Other bacteria for which antibiotic therapies exist, are showing increasing resistance and these include STDs, Haemophilus, Diplococcus and several members of the Enterobacteriaceae.



However, there may be light at the end of the tunnel. The following article shows how IT coupled with diligent research can provide answers to the current issues. I spent the early part of my career specialising in microbiology in pharmaceutical QA and am keen to see that our industry can continue providing antibiotic therapies. I have great hopes that these new approaches will come to fruition in just a few years.

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Of the above-mentioned organisms, there are three that the World Health Organisation has identified as “critical threats”. Now, thanks to some ground-breaking research, scientists may have come up with an antibiotic which can overcome “pharmaceuticals Public Enemy #1”- a bacterium known as Acintobacter baumannii.

Worldwide these “super bugs” (the 2 others are S.aureus, and Ps.aeruginosa) are estimated to cause more than 1,000,000 people per year to die from infections that resist the treatment with our existing armoury of antibiotics.

Not only was this novel antibiotic shown to be extremely powerful, but it was found as a result of research using **artificial intelligence (“AI”).**

The key steps in this work** were as follows:

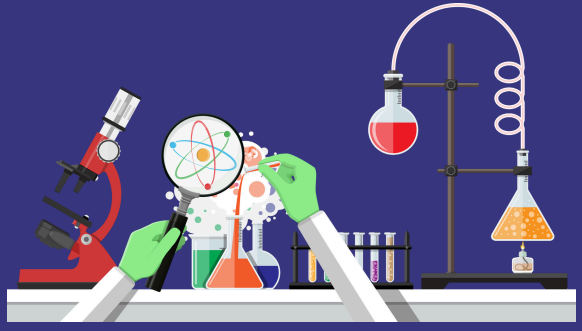
1. Thousands of drugs where the precise chemical structure was known were manually tested on this super bug to see which could slow it down or kill it.
2. This information was fed into the supercomputer so it “learnt” the chemical features of drugs which could hopefully attack the Super bug.
3. The supercomputer was then fed a list of almost 7000 compounds whose effectiveness was unknown. Despite this high number, **within 90 minutes** AI produced a short list of potential compounds, of which 240 were tested in the laboratory.
4. The researchers tested 240 of these in laboratory conditions and found nine potential antibiotics one of which was the unexpectedly potent antibiotic **abaucin** .

These laboratory experiments showed that **abaucin** could treat infected wounds in mice and was able to kill the bacteria in samples from patients. Uniquely the drug only works on **Acintobacter baumannii**. And unlike other existing antibiotics, this drug doesn’t kill other bacteria such as the useful ones in the human gut.

What lies ahead is the standard R&D work to define the synthetic route, work up dosages & product form, and carry out clinical trials. But we can hope that perhaps by 2030 we may no longer fear being infected by this hospital bug. Moreover, the success of this work with AI will spur similar research, **and the other two super bugs are already “in the crosshairs” of researchers.**

Steve Biddulph

(** Results in Nature Chemical Biology)



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Fewer Tablets & Capsules (per person) – Fewer Side Effects

When lunching with some elderly relatives I see them settling down at table with a pillbox by their side ready to comply with their drug regime. “I rattle when I walk” is the joke regarding some folks’ diet of pills and capsules.

Some 20% of Americans and Canadians in the age group 40 -79 take five or more drugs every day. Similarly, about 15% of people in England try to comply with the same size drug regime. For a sizeable minority of these patients this is doing them some harm. A review of overprescribing concluded that at least 10% of prescriptions by England’s GP's and pharmacists should not have been provided.

This issue is termed “polypharmacy”. There have been various studies and estimates of the increase in hospital admissions as a result of adverse reactions to drugs, and a typical figure is almost 20%. A study estimated 150,000 premature deaths per year in USA for this same reason. Polypharmacy creates other less severe problems for patients, for example worry. “Where is the pill box?” or “Did I miss a dose?”. The more drugs a patient takes the greater the chance that they will make a mistake.

Coming soon less of these?

The second problem is that several drugs may affect the same biological pathway. For example, apparent dementia symptoms have been shown to be the result of polypharmacy rather than the actual disease itself. Happily, for some patients, doctors were able to reverse numerous incorrect diagnoses.

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The more pills someone takes the more likely it becomes that some of them will interact in harmful ways, and the number of potential combinations is huge. Clinical trials necessarily are limited to testing one drug at a time. Although old people are the largest group taking multiple products, they are not the young and healthy ones usually necessary in clinical trials.

A further problem is a lack of unified personal health records - prescriptions made by private practitioners may not be visible to public health bodies and vice versa. Also, OTC drug purchases are invisible to GP's.

Some medication should only be taken for a limited time. Problems arise if patients are not be told when to stop taking a drug, or they may forget and continue.

80% of patients are willing to give up a drug if their doctor advises them, and alternatives may be available eg behaviour therapy rather than sleeping pills for insomnia. There are now some online guides to “de-prescribing” such as Medsafer and The Drug Burden Index. Let's hope they are used so more fruits of research can be used properly, and some large healthcare costs avoided.
The Editor

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CHECK OUT the EMA to see what might be coming

By Jose Zapata
Galenisys Pharma Senior Expert. Pharmacist with frontline experience in Quality, Operations & Project Management.
PDD Certified

EMA medicines evaluation UPDATE.

Our articles on research in life sciences implies talking about things that may materialise in one or two decades time. However by looking at the EMAs' "In Tray", we can see what might be arriving on the market in the near future, ie product approvals.

Here I'm going to point to the medicines currently under evaluation. So, let's have a look at the EMAs' workload for the approval (or rejection) of possible new human medicines.
Every month the EMA publishes a list with initial marketing authorisation applications for human medicines currently under evaluation by the Committee for Medicinal Products for Human Use (CHMP).
This list only includes information for medicines whose applications have been validated and for which evaluation has already been started. Generics, biosimilars and duplicates are included.
The Entries are removed from the (pending) list once the medicine has received a positive or negative opinion from the CHMP or when the applicant has withdrawn the application.
We can see details of these as the Agency publishes information on these opinions and withdrawn applications on its website.

As of May 2023, there are 103 applications pending:

- One is from 2020. It's the oldest one on the list - the biologic antineoplasic Bevacizumab, Its evaluation started on December 2020.
- There are still 8 applications pending from 2021; 70 from 2022; & 24 from this year 2023.
- 37 of them are biologicals, 61 are chemicals, 4 radiopharmaceuticals and 1 ATMP (haematological).
- Orphan products are 30 of the total (29%).
- And the generics, hybrids or biosimilars total 33 (32%).

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In April 2023 the pending list totalled 111 applications, ie in the last month the “queue” reduced by 8 medicines.

If we compare with the list from previous years, we can observe that in general the numbers do not differ too much from year to year, but the queue has been reduced by about 10%; as there were 112 pending applications in December 2022, & 129 in December 2021.

We consider that this information is valuable in understanding which healthcare research & innovation is coming to fruition in Europe. This defines which companies, pharmaceutical technologies & product forms are involved, and where facilities, expertise & experience will be needed in the near future.

Galenisys experts continue to support innovative companies in preparing dossier submissions, facilities design & construction, and staff training, all of which are needed to deliver the emerging healthcare products.
Don’t hesitate to contact us.
José Zapata

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New Products that need to come

It's stating the obvious to note that the ongoing healthcare research we've mentioned needs to be paid for, & that money needs to come from somewhere. So cashflow is also a guide to "what's coming".

The recent expenditure of the large pharma multinationals is notable in this context:

- Merck (USA) is spending $10.8 billion on the acquisition of Prometheus Biosciences.This biotech company in California has no profits and no approved drugs, but it does have a very promising late-stage clinical trial drug to treat ulcerated colitis, Crohn's disease, and other unpleasant autoimmune diseases.

- In March Pfizer agreed to pay $4 billion for Seagen a loss-making cancer biotech company, and in April GSK agreed to buy Bellus Health a Canadian biotech firm with a promising treatment for chronic coughs.

So why are these multinationals splashing the cash? One key reason is they need to replace products which will "fall off the patents cliff" by the end of this decade.

This of course will radically reduce their income and profitability. Industry wide patents for more than 190 drugs will expire by 2030, representing more than $200 billion of sales. So, bosses are spending big to plug the gaps, on new drugs which possess replacement potential.

One estimate of the value of takeovers in the pharma / life sciences industry is that it could reach $275 billion in 2023, a large increase from last year.

Fortunately for these drug majors they have money in the bank, with $1.4 trillion waiting to be deployed.

The Editor

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