Learn Chemistry

Business Skills and Commercial Awareness for Chemists

Drug Reprofiling Scenario

Developed by the University of York and University of Warwick

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Salbutamol – a drug reprofiling opportunity?

Background

Our company's team of biochemists have identified that the beta-adrenoreceptor agonist salbutamol unexpectedly binds to reverse transcriptase related proteins. The possibility that salbutamol interacts with proteins with reverse transcriptase activity was of interest, since retroviruses such as HIV use this enzyme during the infection process. This alerted us to an opportunity to "reprofile" the drug. Drug reprofiling, also described as drug repositioning, drug repurposing or therapeutic switching, is an attractive strategy for the development of new pharmaceutical drugs, since bringing existing drugs to market in a new therapeutic setting carries less of a regulatory burden than developing a new chemical entity[1].

Results

Figure 1 shows the activity of an HIV-1 reverse transcriptase in the assay we selected[2] (EnzChek, Invitrogen, using HIV-1 reverse transcriptase). When the known reverse transcriptase inhibitor quercetin was added, the fluorescence reading indicated just 10% background activity in comparison to undrugged reverse transcriptase. In order to compare results read from multiple plates, this background reading was normalised to 0%, with the undrugged reverse transcriptase output normalised to 100%. We also included two other beta-adrenoreceptor agonists, two beta blockers and one randomly selected drug from our collection that is not categorised as beta-adrenoreceptor interactor, allopurinol. As expected, allopurinol had no significant effect as compared with our 100% control (no drug added). Surprisingly, four of the five beta-adrenoreceptor agonists and blockers led to significant *increases* in reverse transcriptase activity in this assay. At 100 μM, whereas quercetin completely inhibits the activity, salbutamol enhances it by over half. While unexpected, we should note that our chemical genomics assay identifies only interaction and cannot predict the effect of any binding

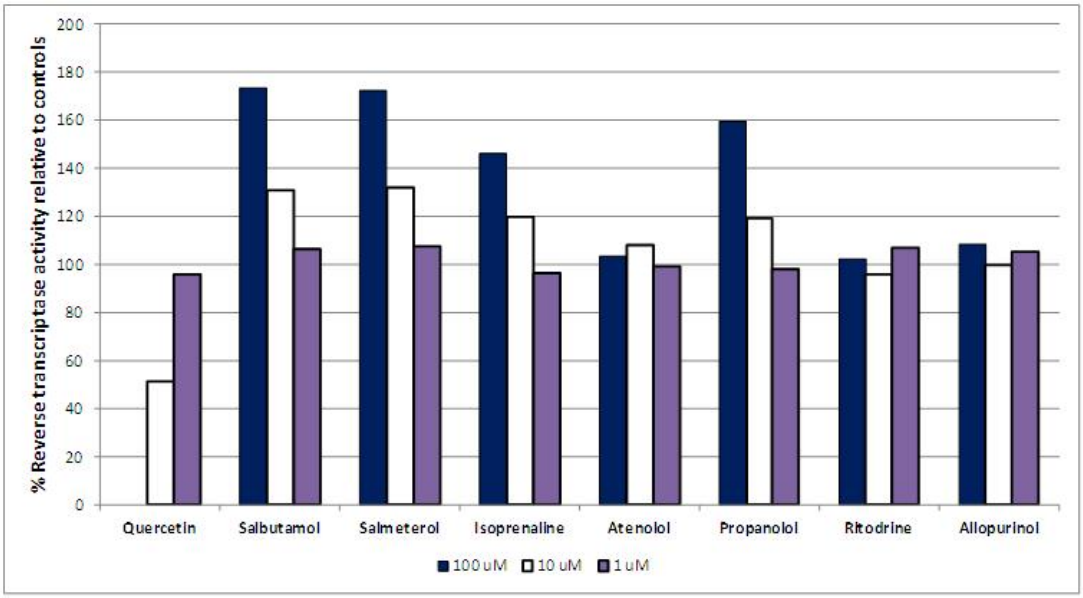

Figure 1 Activity of an HIV-1 reverse transcriptase in the presence of five beta-adrenoreceptor agonists and two other drugs (ritoline and allopurinol) relative to a 100% control of 'no drug present', and a 0% control of 100 uM quercetin (a known reverse transcriptase inhibitor).

Task

Your task is to advise the company management on whether there is an opportunity to "reprofile" salbutamol, or a related rug, as an HIV therapy. You should consider:

- the scientific case for a drug that increases reverse transcriptase activity being used as an HIV therapy;
- the market opportunity for using this existing drug as a new therapy for HIV;
- the IP landscape – would it be possible to patent salbutamol or an analogue in the major markets?
- an outline of regulatory processes that would need to be completed to bring an existing drug to market in a new therapeutic indication, specifically HIV.

Please present your recommendations in a report/business plan, including a ca. 150 word executive summary.

Assessment

If your report is to be assessed as part of your coursework, please consult your tutors for the assessment criteria.

References

1. Sleigh, S. H. and Barton, C. L. Repurposing Strategies for Therapeutics. Pharm. Med. **24**, 151–159 (2010).
2. Invitrogen EnzChek® Reverse Transcriptase Assay Kit (E-22064).