ORIGINAL ARTICLE

Predicting the Spectrum of Biological Activity, Adverse Effects, and Toxicity of Aceclofenac Using Prediction of Activity Spectra for Substances Software

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Abstract

Background: The present investigation was conducted to assess the overall biological potential of existing therapeutic agents and drug-like organic compounds based on their inherent physicochemical and structural characteristics. Recent advances in cheminformatics and bioinformatics have significantly enhanced the application of *in silico* techniques for predicting the biological activities of organic molecules, making computational prediction an important strategy in modern drug discovery and medicinal chemistry. Prediction of Activity Spectra for Substances (PASS) is a web-based computational platform developed for the simultaneous prediction of multiple pharmacological and toxicological properties of drug-like compounds. The predicted biological profile is primarily associated with the molecular structure and physicochemical attributes of the compound; therefore, the activity spectrum is considered an intrinsic property of a molecule. In the present study, the biological activities and possible toxicological effects of the analgesic drug aceclofenac were predicted using PASS software to evaluate its pharmacological potential and drug-likeness characteristics. **Result:** The prediction results demonstrated significant Pa values for several activities, including CYP2J2 substrate (0.951), CYP2J substrate (0.945), antipyretic activity (0.876), HIF1A expression inhibition (0.857), chlordecone reductase inhibition (0.827), and treatment of phobic disorders (0.826). These findings indicate the potential anticancer, anti-inflammatory, antimicrobial, antipyretic, anxiolytic, and antidepressant effects of aceclofenac. The software also predicted several adverse and toxic effects, such as anemia (0.966), gastrointestinal hemorrhage (0.958), peptic ulcer (0.921), nephrotic syndrome (0.910), and hepatitis (0.913), which suggests the possibility of severe gastrointestinal, renal, and hepatic complications associated with this drug. Further *in vitro* and *in vivo* investigations are necessary to validate the predicted pharmacological and toxicological activities of this compound.

Key words: Aceclofenac, Analgesic agent, Drug repurposing, *In silico* prediction, PASS

INTRODUCTION

Prediction of Activity Spectra for Substances (PASS) is a computational software system developed to evaluate the broad biological potential of organic drug-like molecules.[1] The software simultaneously predicts multiple biological activity categories based on the molecular structure of the compound.[1,2] Consequently, PASS can be effectively utilized to estimate the biological activity profile of virtual compounds before their synthesis and experimental biological evaluation.

The PASS platform predicts the biological activity profile of a test molecule using its structural representation in formats such as SMILES, InChIKey, MOL, or SD files. Predictable biological activities include pharmacotherapeutic effects, biochemical mechanisms of action, toxicological properties, metabolic interactions, regulation of gene expression, and transporter-associated activities. Examples of these effects include antiarrhythmic effects, cyclooxygenase inhibition,

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carcinogenicity prediction, CYP450 inhibition, VEGF expression inhibition, and P-glycoprotein substrate identification.

The prediction system is based on structure–activity relationship analysis derived from more than 250,000 biologically active compounds,[1] including marketed drugs, lead molecules, drug candidates, and toxic substances. PASS utilizes a large training dataset to provide an objective estimation of whether a molecule is likely to exhibit a specific biological activity. The software is accessible through the official PASS Online platform. [http://www.way2drug.com/PASSOnline/].[1-12]

The PASS training dataset currently includes approximately 6825 biological activities, including pharmacological effects, mechanisms of action, toxic manifestations, metabolic properties, effects on gene expression, and transporter-related activities.[1] Certain activities represented by insufficient training examples were excluded from the list of predictable activities to maintain the reliability of the prediction model.[1]

The process of PASS development and use is shown in Figure 1 below.

METHODOLOGY

The biological activity spectrum of aceclofenac was predicted using the PASS version 2.0, developed by the Department for Bioinformatics,[1] Laboratory for Structure–Function Based Drug Design, Institute of Biomedical Chemistry, Moscow, Russia. PASS version 2.0, introduced in 2011, was employed to evaluate the pharmacological and toxicological profiles of the selected compounds.

An account was created on the official PASS Online website, and the prediction process was initiated using the "Go to PASS Prediction" option. The chemical structure of aceclofenac was submitted in SDF or MOL file format obtained from the PubChem database.[1] Alternatively, the molecular structure can be generated using Marvin JS software. After loading or drawing the structure, prediction was performed by selecting the "Predict" option within the PASS interface is shown in the figure 2.

RESULTS

The prediction results were expressed as Pa (probability of activity) and Pi (probability of inactivity) values for each predicted biological activity and toxicological effect associated with aceclofenac.

PASS predictions for aceclofenac across all possible pharmacological activities, adverse effects, and toxic effects were performed, and the results are presented in Table 1.

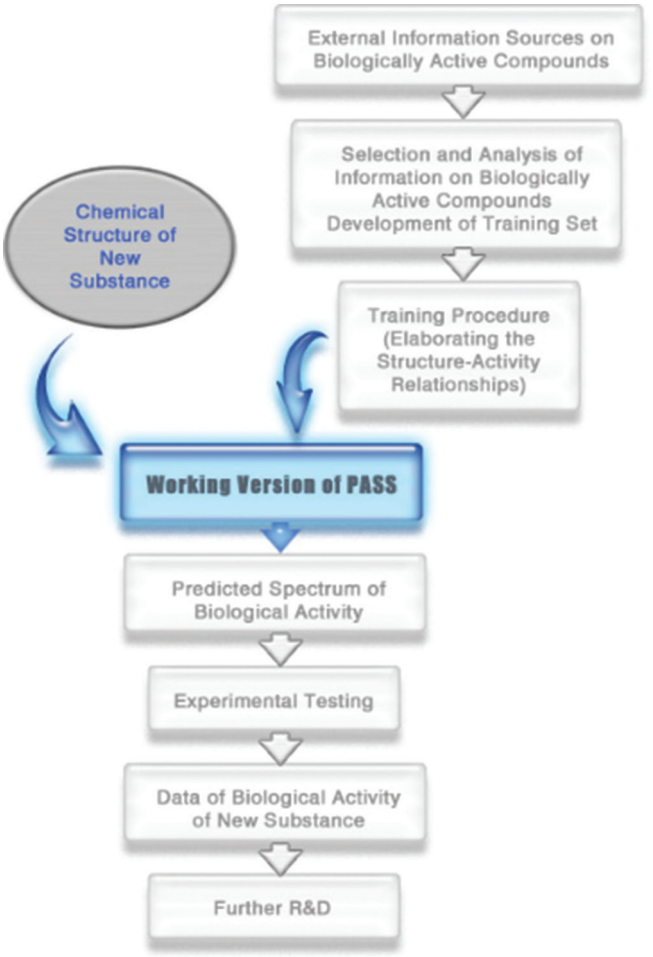

Figure 1: Depicting the process of prediction of activity spectra for substance development and use. Source: [http://www.way2drug.com/PASSOnline/]

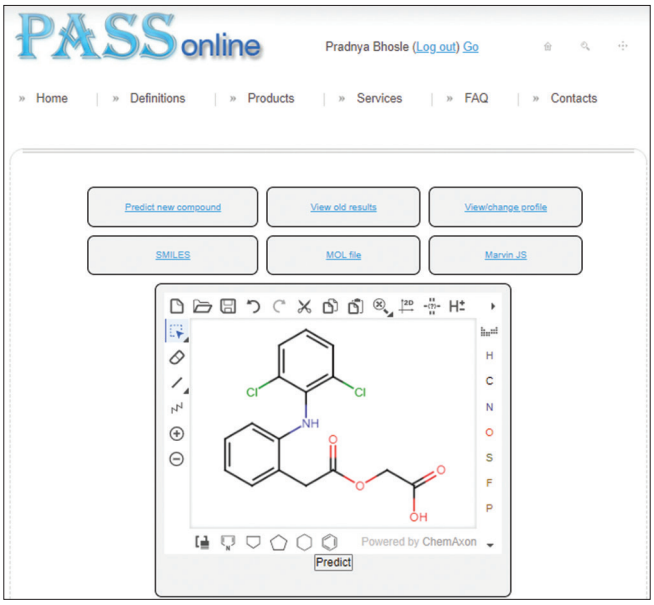

Figure 2: Structure of aceclofenac for the prediction of activity spectra for substances prediction

Table 1: Summary of the prediction of biological activities of aceclofenac

Pa	Pi	Activity
0.951	0.002	CYP2J2 substrate
0.945	0.002	CYP2J substrate
0.876	0.003	Antipyretic
0.857	0.008	HIF1A expression inhibitor
0.827	0.015	Chlordecone reductase inhibitor
0.826	0.024	Phobic disorders treatment
0.798	0.002	Cyclooxygenase 3 inhibitor
0.800	0.007	Anti-inflammatory
0.787	0.007	Linoleate diol synthase inhibitor
0.776	0.008	Oxidoreductase inhibitor
0.758	0.015	GST A substrate
0.727	0.001	Hyaluronic acid agonist
0.721	0.003	CYP2C18 substrate
0.717	0.004	CYP2E1 inhibitor
0.722	0.010	Lipid metabolism regulator
0.739	0.033	Antieczematic

Table 2: Summary of the prediction of adverse and toxic effects of aceclofenac

Pa	Pi	Adverse and toxic effects
0.966	0.004	Anemia
0.958	0.001	Gastrointestinal hemorrhage
0.921	0.002	Ulcer, peptic
0.910	0.003	Nephrotic syndrome
0.913	0.006	Hepatitis
0.895	0.001	Papillary necrosis
0.900	0.011	Conjunctivitis
0.889	0.002	Ulceration
0.902	0.017	Toxic, respiration
0.880	0.004	Gastrointestinal disturbance
0.873	0.004	Allergic contact dermatitis
0.863	0.003	Nephritis
0.859	0.014	Hepatotoxic
0.837	0.010	Asthma
0.824	0.003	Ulcer, gastric

DISCUSSION

Biological activity arises from the interaction between a chemical compound and its corresponding biological target, which is largely influenced by the molecular structure[8,11] and physicochemical properties of the compound.[1,2] The biological activity spectrum of a molecule represents the complete range of pharmacological, biochemical, and toxicological effects associated with that compound, regardless of the experimental methods used for its determination. Therefore, the biological activity spectrum may be regarded as an intrinsic molecular characteristic that is primarily dependent on structural and physicochemical attributes.

Biologically active compounds can have both therapeutic and undesirable effects. While certain activities contribute to disease treatment and provide clinical benefits, others may result in adverse reactions or toxic manifestations. The overall combination of these effects is collectively referred to as the biological activity spectrum of a substance in table 1.

In the PASS prediction system, the Pa value represents the probability that a compound exhibits a particular activity, whereas the Pi value indicates the probability of inactivity.[1] The Pa score reflects the structural similarity of the test molecule to compounds categorized as active within the training dataset. These predictive values assist researchers in identifying promising pharmacological activities while simultaneously estimating the risk of negative experimental outcomes. The selection of activities for further investigation depends on the balance between the novelty of action, experimental feasibility, and the likelihood of successful biological validation.[3,6]

CONCLUSION

The present investigation successfully evaluated the biological activity profile and toxicological potential of aceclofenac using the PASS software.[8,9] The prediction results demonstrated high Pa values for several pharmacological activities, including CYP2J2 substrate activity (0.951), CYP2J substrate activity (0.945), antipyretic activity (0.876), HIF1A expression inhibition (0.857), chlordecone reductase inhibition (0.827), treatment of phobic disorders (0.826), cyclooxygenase inhibition (0.798), and anti-inflammatory activity (0.800). These findings suggest that aceclofenac may possess significant anticancer, anti-inflammatory, antimicrobial, antipyretic, anxiolytic, and antidepressant properties, in addition to its established analgesic activity.[2,6,10]

The study also predicted several clinically significant adverse and toxic effects associated with aceclofenac, including anemia, gastrointestinal hemorrhage, peptic ulceration, nephrotic syndrome, hepatitis, allergic contact dermatitis, nephritis, gastrointestinal disturbances, and hepatotoxicity. These findings indicate the possibility of serious gastrointestinal, renal, and hepatic complications associated with the prolonged or inappropriate use of the drug.

FUTURE SCOPE

The predicted pharmacological activities obtained from the PASS analysis indicate that aceclofenac may serve as a

promising candidate for drug repurposing studies. Further molecular docking studies, *in vitro* screening, and *in vivo* pharmacological evaluations are required to validate the predicted anticancer, anti-inflammatory, antimicrobial, antipyretic, anxiolytic, and antidepressant activities of this compound.

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