

Task-Specific Refinement of a Multitask AI Model for Blood–Brain Barrier Prediction

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ABSTRACT

ADMET (absorption, distribution, metabolism, excretion and toxicity) issues remain one of the main reasons why otherwise promising small molecules fail late in the pipeline. Being able to screen these liabilities early, directly from structure, is therefore a practical way to de-risk discovery. In this work we take an existing ADMET-AI multitask graph neural network as a baseline and develop a variant specifically strengthened for blood–brain barrier (BBB) permeability prediction. The original ADMET-AI model, trained on 41 ADMET datasets from the Therapeutics Data Commons and RDKit descriptors, already delivers broad ADMET coverage, but its performance on BBB was limited by the size and heterogeneity of the BBB data. We therefore integrated additional BBB datasets from the literature and retrained/fine-tuned the model on this expanded BBB subset. On two external BBB benchmarks, DeePred and Zhuang, the adapted model increased correct classifications from 87% to 95% and from 92% to 98%, respectively, with AUC values >0.90 in both cases, indicating more reliable separation of BBB-permeable versus non-permeable compounds. Because inference remains fast and deployable locally, the approach preserves the practicality of the original model while delivering a targeted improvement on a CNS-critical ADMET endpoint.

INTRODUCTION

Many promising drug candidates fail during development because of ADMET issues, including poor absorption, distribution, metabolism, excretion or toxicity. For drugs that act on the central nervous system, permeability across the blood brain barrier is especially important, since compounds that cannot reach the brain are unlikely to be effective. Deep learning methods such as ADMET AI use graph neural networks to predict several ADMET properties directly from molecular structure. Their performance depends strongly on the amount and quality of available data. In the original ADMET AI model, predictions for blood brain barrier permeability were limited by the small size and heterogeneity of the training datasets. The aim of this work is to improve blood brain barrier (BBB) prediction by integrating additional data from the literature and fine tuning the model on this expanded dataset. This study highlights how data enrichment, rather than architectural complexity, can unlock the full potential of graph neural networks for predictive pharmacology.

METHODS

The starting point was the ADMET AI model, a multitask graph neural network designed to predict several pharmacokinetic and toxicity endpoints from molecular structure. Each molecule was represented as a graph combined with a set of RDKit descriptors, and the model was originally trained on forty-one ADMET datasets from the Therapeutics Data Commons. To strengthen prediction of blood brain barrier permeability, additional datasets were collected from the literature and merged with the original training data. Duplicates and inconsistent entries were removed, and all molecular structures were standardized to ensure compatibility. The model was then fine tuned on this expanded blood brain barrier subset while maintaining the multitask setting to preserve information learned from related endpoints. Performance was evaluated on two external benchmarks, the DeePred and Zhuang datasets, using accuracy and area under the ROC curve as primary metrics. Inference time and computational cost were also recorded to confirm that the adapted model remained suitable for local deployment.

RESULTS

The adapted model achieved higher accuracy on both external benchmarks compared with the original ADMET AI. On the DeePred dataset, the proportion of correctly classified compounds increased from 94 percent to 97.5 percent. On the Zhuang dataset, accuracy rose from 93 percent to 96.3 percent. In both cases, the area under the ROC curve exceeded 0.90, indicating reliable separation between permeable and non permeable compounds. Consistent with these results, per-class precision improved from 86.68% to 95.22% for Class 0 and from 97.33% to 98.60% for Class 1, with predicted-probability distributions showing clearer separation and reduced overlap near the decision threshold. The model retained its original inference speed and could be executed locally without additional computational requirements. These results confirm that expanding the training data and applying targeted fine tuning can substantially improve prediction performance without increasing model complexity.

CONCLUSION

Expanding and refining the data used for training led to a clear in predicting blood brain barrier permeability. The results suggest that the amount and quality of data remain key factors for progress in ADMET prediction. Graph neural networks can make full use of new data as it becomes available, offering a practical path to more accurate and generalizable models. Continual integration of new public datasets may further enhance performance across other ADMET endpoints, supporting earlier and more reliable decisions in drug discovery.

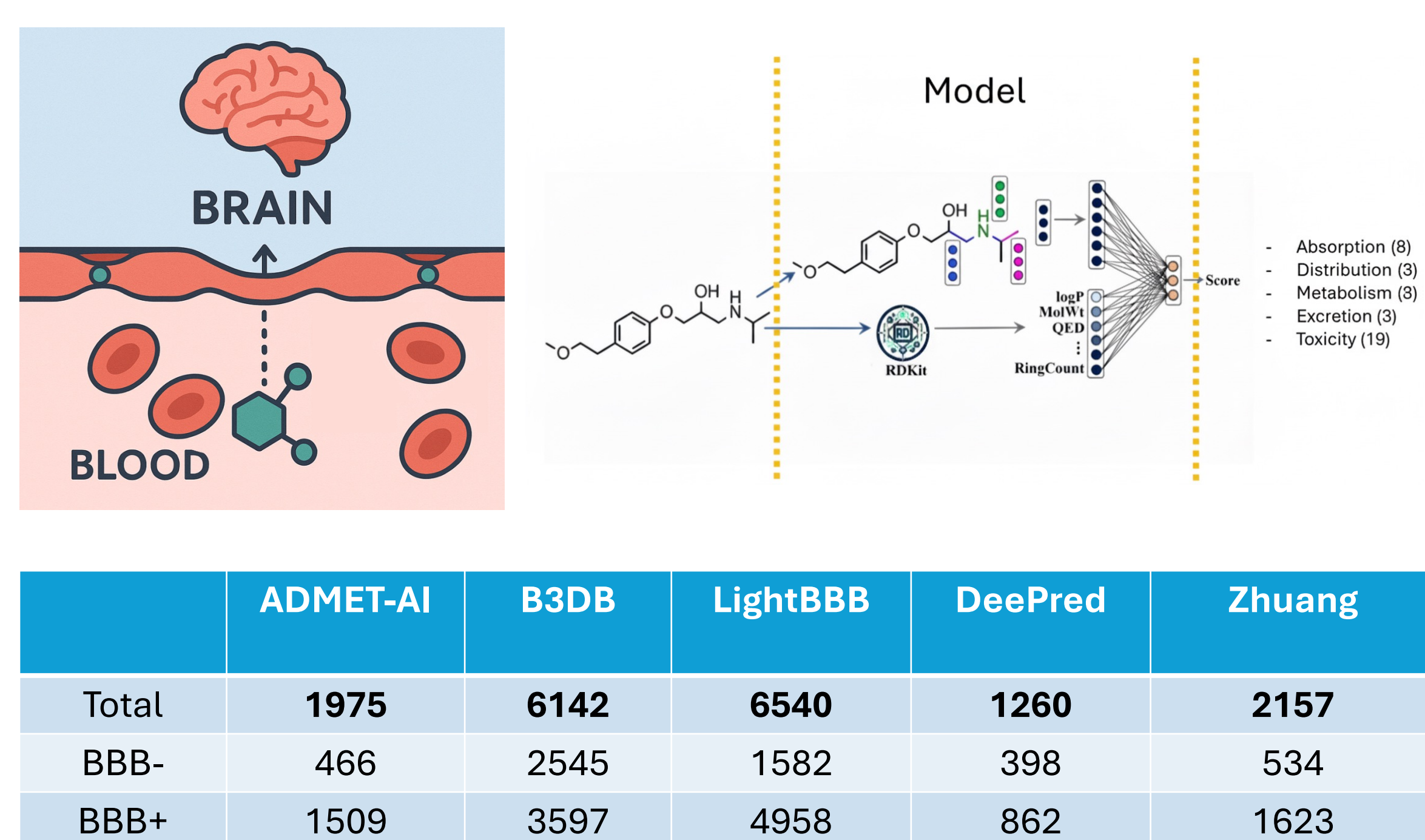


Figure 1 Workflow for Blood–Brain Barrier Prediction Using ADMET-AI. Overview of the data sources, model architecture, and workflow used to predict blood–brain barrier permeability with the fine-tuned ADMET-AI model

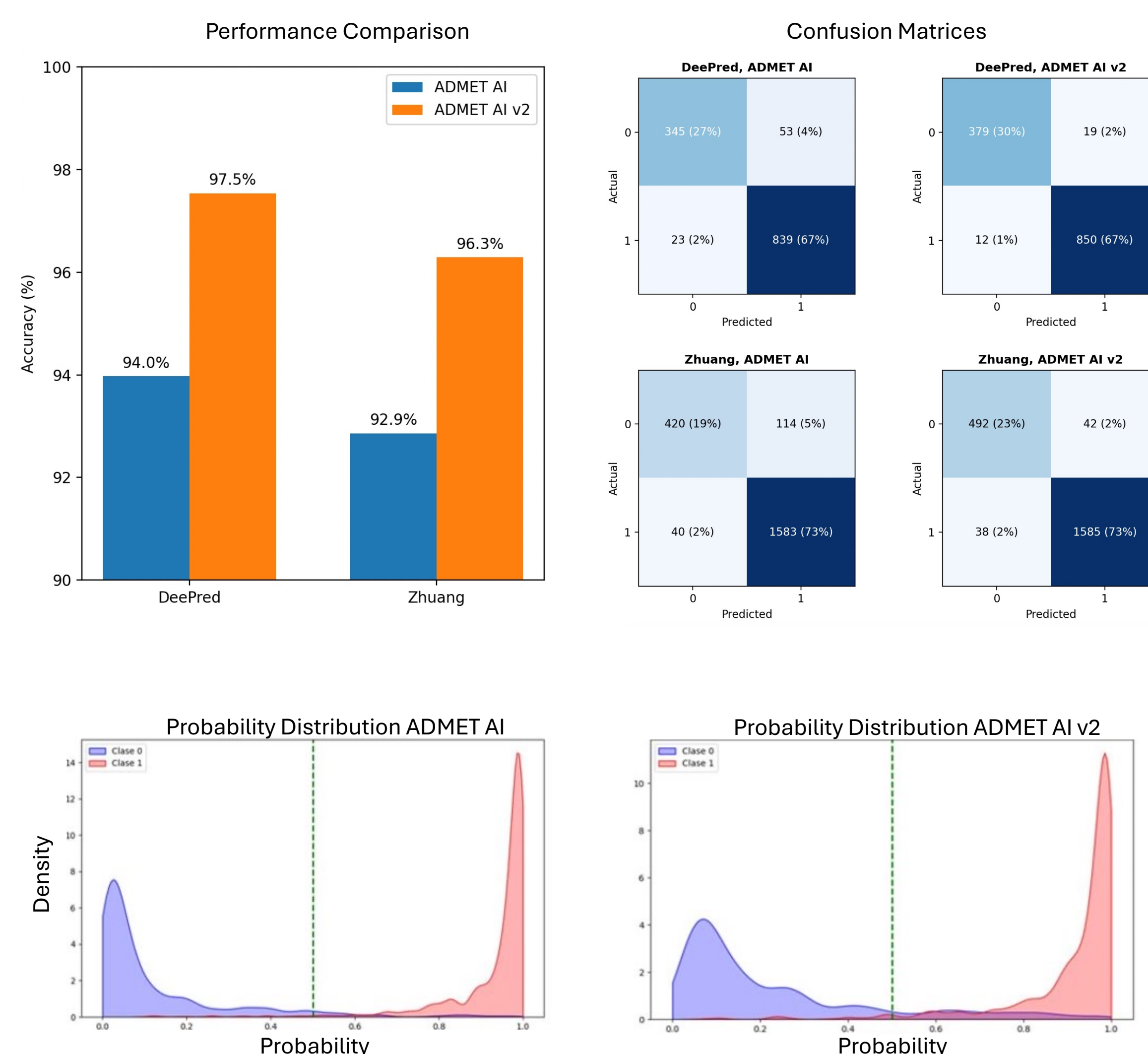


Figure 2. Performance Evaluation on External BBB Benchmarks. Comparison of baseline and fine-tuned ADMET-AI models on the DeePred and Zhuang datasets, showing higher accuracy and fewer misclassifications after BBB-specific training