The research advances of drugs and their targets

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Abstract

Background: Drug targets are important for mechanism-based drug discovery, so it is important to have a comprehensive understanding of drugs and their targets. Current research: There are so many researchers who have analyzed the number and classification of drugs and their targets. However, due to the continuous approval of drugs and the inconsistency of drug target definitions, there are some controversy about the number and progress of drugs and their targets in the past few years. Research purposes: In this study, we summaried the approcal drugs through the in-depth research of the FDA Orange Book from the US FDA official websiteand explore the research progress of the approval drugs and their targetsaccording to its corresponding targets and indications, which is benefical to the research and development of drugs and their targets.

Keywords

Pharmacostatistics, Approval drugs, Targets, Indications.

1. Introduction

It usually spends about eight years before the US FDA approved the drugs, which require some processes including pre-clinical studies, clinical trials, and FDA approval [1]. According to the reports, in this process of pre-clinical studies, there are thousands of lead compounds initially, but only ten candidates could enter the process of clinical trial. Finally, there is only one drug could be approved by the FDA, which indicates that the success rate of drug development is pretty lower [2]. In addition, the cost of research and development of drugs is also very large, including excessive time cost and excessive resource consumption. Therefore, it is extremely urgent for researchers to comprehensively study the processes of drug discovery, which is beneficial to reduce its cost [3].

At present, there are many methods for drug development and discovery, such as some methods based on mechanisms, fragments, and models, respectively [4]. With the advent of the post-gene era, a large number of targets have been exploited [5], and the target is the biomolecule with which the drug acts to produce therapeutic effects, which is the key to therapeutic indications [6]. In 2000, James Black proposed that the best way to discover new drugs is based on old drugs, so an in-depth study of the mechanism for drug approval is important for the development of new drugs [7]. Therefore, mechanism-based drug development has become increasingly important due to the emergence of a large number of targets [8]. In the mechanism-based drug development process, the identification and confirmation of drug targets is the first decisive factor [9]. Research on targets can promote drug development and increase the success rate of drug development [10]. However, the definition of drug targets by researchers is ambiguous, so the specific number of successful targets is different in recent years [11-12]. Therefore, in this study, we analyze the number of approval drugs and their targets, and expounds the research progress of drugs and their targets according to their corresponding therapeutic diseases, which helps researchers to comprehensively research approval drugs and their targets, which provides a new direction for drug development.

2. Data Collection

First, we downloaded the Orange Book from the US FDA official website, which includes all FDA-approved drugs including new molecular entity drugs, biopharmaceuticals, and their generic drugs.

Based on their classification, we selected new molecular entity drugs and biopharmaceuticals as our research objects, for the reason that the mechanism of action of generic drugs is the same as its corresponding new drug) [13]. Secondly, the corresponding indications and targets of all new molecular entity drugs were collected separately for the instructions of these drugs on the FDA's official website for subsequent analysis. Finally, the recorded targets were revalidated according to the therapeutic target database [6] (TTD), the Drugbank database [14], and literature review. Furthermore, the most accurate target information was obtained through this step [15].

3. Analysis and Results

In 2006, Overington proposed that all FDA drugs created their therapeutic effects through 324 protein targets [15]. Moreover, it is helpful to analyze these successful targets for identifying new drug targets [17-18]. Therefore, we conduct research and analysis on all approved drugs and their targets.

3.1 Approval drugs and their targets

As shown in Table 1, based on the in-depth analysis of the FDA Orange Book, two databases, and the literature review, we have found 1,777 approved drugs targeted 529 targets before 2018, including 446 human targets and 83 non-human targets. In addition, the earliest approved drug was in 1939. The number of approved drugs per year from 1939 to 2018 were shown in the figure 1. It can be seen that the number of drugs were approved in 1982 is the most with 80 drugs. Furthermore, it is obvious that the overall trend of the number of approval drugs is rising due to the advancement and the development of technology [19].

In addition, in this study, we counted the number of targeted drugs of each target and discovered the top 10 targets aimed by drugs, which presented in Figure 2. As can be seen from Figure 2, the Histamine H1 receptor corresponds to 41 drugs, which is the most one and followed by the Dopamine D2 receptor corresponding to 39 drugs.

Table 1 The number of all approval drugs and their targets

Drugs	Targets	Human Targets	Non-Human Targets
1777	529	446	83

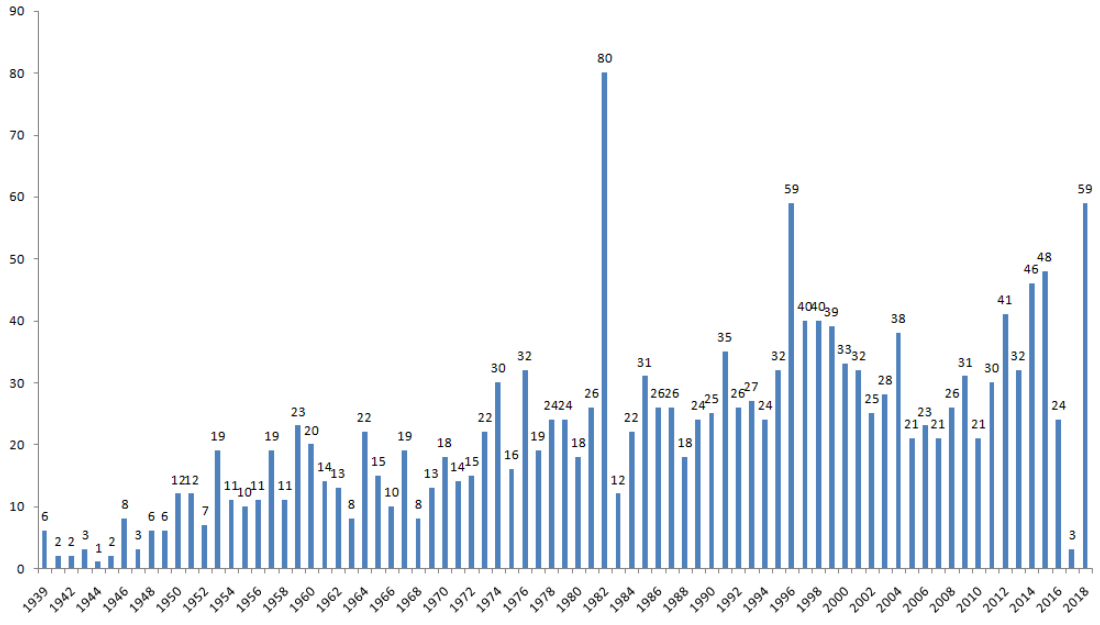

Fig. 1 The approval drug among 1939 to 2018

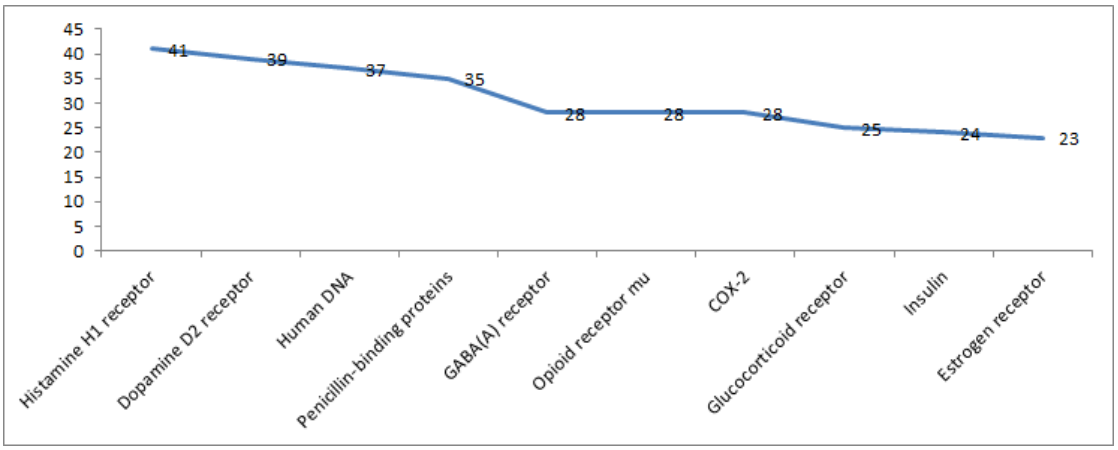

Fig. 2 The top 10 targets aimed by approval drugs

The analysis of Approval drugs based on Disease

ICD-10 is the 10th edition of the Medical Classification List of the World Health Organization (WHO) for the International Statistical Classification of Diseases and Related Health Problems (ICD). There are 22 major categories, including diseases, signs and symptoms, abnormal findings, complaints, social conditions and injuries or diseases caused by external causes. We corresponded to the disease in the ICD according to the name of the disease, and found that all approved drugs were distributed in 20 ICD categories, including A00-B99, infectious and parasitic diseases; C00-D49, tumor; D50 - D89, blood, hematopoietic organs and certain diseases involving immune mechanisms; E00-E90, endocrine, nutritional and metabolic diseases; F01-F99, mental and behavioral disorders; G00-G99, neurological diseases; H00-H59 diseases of the eye and adnexa; H60-H95, diseases of the ear and mastoid; I00-I99, circulatory diseases; J00-J99, respiratory diseases; K00-K93, digestive diseases; L00-L99, skin and subcutaneous tissue diseases; M00-M99, musculoskeletal system and connective tissue disease; N00-N99, genitourinary system disease; O00-O99, pregnancy, childbirth and puerperium; P00-P96, originating from some cases of perinatal; Q00-Q99, congenital malformations, deformations and chromosomal abnormalities; R00-R99, symptoms, signs and clinical and laboratory abnormalities, not elsewhere classified; S00-T98, Injury, poisoning and certain other consequences of external causes; Z00-Z99, factors influencing health status and contact with health services.

The corresponding number of approval drugs of these 20 disease categories were shown in the figure 3. As shown in figure 3, the number of drugs that are used to the treat infectious diseases and parasites is the highest, which consists of 252 drugs and followed by the treatment of tumor, which including 200 drugs. Moreover, the number of drugs were used to cure endocrine, nutritional as well as metabolic diseases, and circulatory diseases are approximately equal with about 180 drugs, respectively.

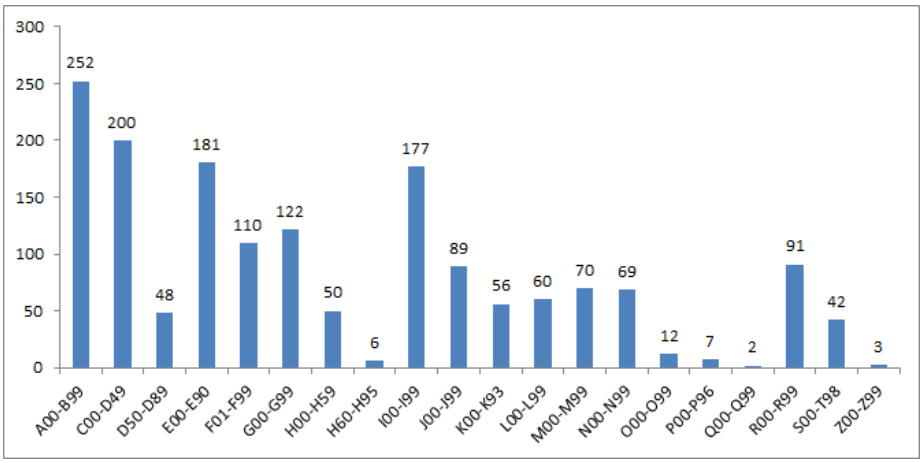

Fig. 3 The classifications of approval drugs based on the corresponding disease

The analysis of Approval drugs based on Disease

The target is classified according to the disease that their corresponding drugs treat. The number of targets of these 20 disease categories were shown in the Figure 3. As shown in Figure 3, the number of targets corresponding to the infectious diseases as well as parasites is the same as that of tumor with 111 targets, which is followed by the number of targets that were used to treat endocrine, nutritional and metabolic diseases, including 101 targets. Furthermore, the number of targets of circulatory diseases and neurological diseases are 69 and 68 respectively.

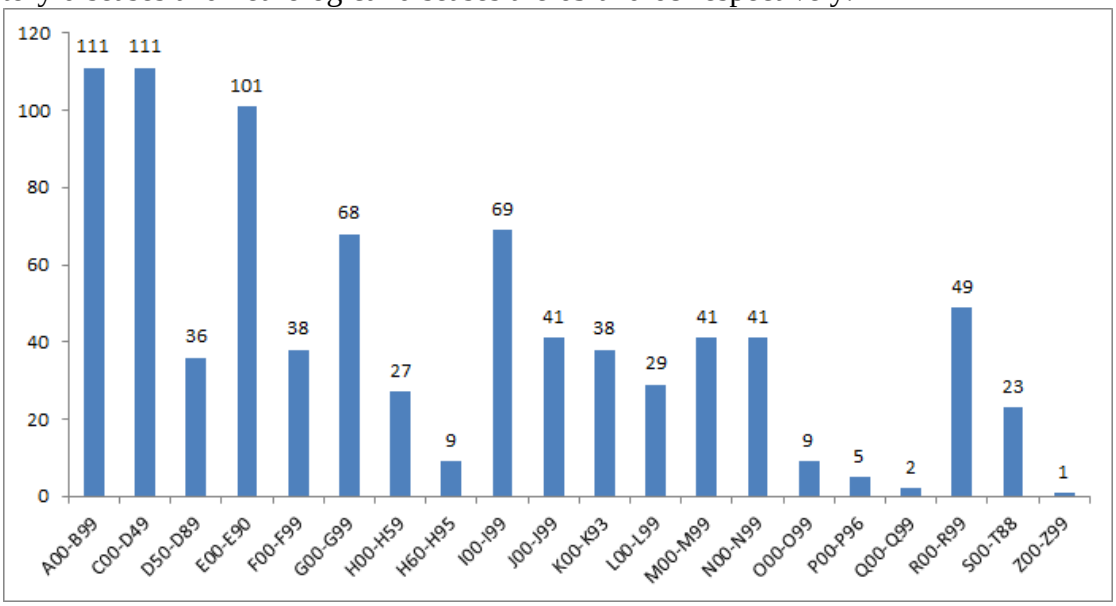

Fig. 4 The classifications of drug targets based on the corresponding disease

4. Summary

This study provides the number of all drugs and their targets approved by the US FDA before 2018, and points out the top 10 targets with the largest number of drugs. Among the top 10 targets, only one is a non-human target (Penicillin-binding proteins), and the rest are human targets. It can be seen that human targets are more likely to have druggable properties, and researchers can pay more attention to the targets corresponding to a lot of drugs, which benefit for improving the success rate of drug development. In addition, we classify drugs and their targets based on disease, which is helpful for researchers to research the drugs and targets according to the specific disease [20], and reducing drug development costs.

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