A semantic relationship mining method among disorders, genes, and drugs from different biomedical datasets

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Abstract

Background: Semantic web technology has been applied widely in the biomedical informatics field. Large numbers of biomedical datasets are available online in the resource description framework (RDF) format. Semantic relationship mining among genes, disorders, and drugs is widely used in, for example, precision medicine and drug repositioning. However, most of the existing studies focused on a single dataset. It is not easy to find the most current relationships among disorder-gene-drug relationships since the relationships are distributed in heterogeneous datasets. How to mine their semantic relationships from different biomedical datasets is an important issue.

Methods: First, a variety of biomedical datasets were converted into RDF triple data; then, multisource biomedical datasets were integrated into a storage system using a data integration algorithm. Second, nine query patterns among genes, disorders, and drugs from different biomedical datasets were designed. Third, the gene-disorder-drug semantic relationship mining algorithm is presented. This algorithm can query the relationships among various entities from different datasets.

Results and conclusions: We focused on mining the putative and the most current disorder-gene-drug relationships about Parkinson’s disease (PD). The results demonstrate that our method has significant advantages in mining and integrating multisource heterogeneous biomedical datasets. Twenty-five new relationships among the genes, disorders, and drugs were mined from four different datasets. The query results showed that most of them came from different datasets. The precision of the method increased by 2.51% compared to that of the multisource linked open data fusion method presented in the 4th International Workshop on Semantics-Powered Data Mining and Analytics (SEPDA 2019). Moreover, the number of query results increased by 7.7%, and the number of correct queries increased by 9.5%.

Keywords: Semantic relationship mining, Data integration, Disorder-gene-drug relationship
Background
Semantic web technology has been applied widely in the biomedical informatics field. The resource description framework (RDF) data model is commonly used to represent data in the database. A uniform resource identifier (URI) and character strings are used to represent different entities and the relationships between entities. These semantic datasets are published online and can be accessed via the HTTP protocol and are also known as linked open datasets [1]. For example, the Life Sciences dataset is one of the most important parts of Linked Open Data Cloud [2]. This database consists of 339 RDF datasets, including 234 BioPortal datasets, 35 Bio2RDF datasets, and 70 other datasets. Together, they contain over 30 billion semantic relationships. Furthermore, a vast number of semantic relationships has been extracted from biomedical literature databases with unstructured natural language texts (e.g., MEDLINE) [3, 4]. The other existing biomedical datasets include gene-related, disorder-related, and drug-related databases. For example, PharmGKB (https://www.pharmgkb.org) [5] is a database consisting of drugs, clinical guidelines, and gene-drug and gene-phenotype relationships. The UniProt (https://www.uniprot.org/) [6] database aims to provide comprehensive and high-quality resources on protein sequences and functional information. This database comprises UniProtKB, UniParc, UniRef, and the Proteomes dataset. The Kyoto Encyclopedia of Genes and Genomes (KEGG, https://www.genome.jp/kegg) database is a professional knowledge base for the biological interpretation of large-scale molecular datasets, such as genomic and metagenomic sequences [7]. The Semantic MEDLINE Database (SemMedDB) [3] (https://skr3.nlm.nih.gov/SemMedDB/index.html) is a repository of semantic predications (subject-predicate-object triples) from MEDLINE citations (titles and abstracts). This database currently contains approximately 98 million predictions from all PubMed citations (approximately 29.1 million citations, processed using MEDLINE BASELINE 2019) [8]. Over 3000 papers are added to MEDLINE every day. Therefore, new semantic relationships are constantly added to SemMedDB.

In recent decades, continuous effort has been directed to mining semantic relationships from biomedical literature text with machine learning approaches. Conditional random field (CRF) and support vector machines (SVM) have been used to mine relationships [9–11]. In [12], a new semisupervised learning method based on hidden Markov models is proposed to extract the disease candidate genes from the human genome. This method predicts genes by positive-unlabeled learning (PU-Learning). In [13], a verb-centric approach is proposed to extract relationships without a training dataset. In [14], Kilicoglu H et al. extend a rule-based, compositional approach that uses lexical and syntactic information to predict relationships.

An increasing number of graph-based mining techniques are being applied to characterize the semantic relations in semantic relation extraction tasks [15–17]. In [18], graph theory and natural language processing techniques are applied to construct a molecular interaction network to extract relationships automatically.

Deep learning models have been adapted to extract semantic relations for the biomedical domain. Moreover, this approach achieves high performance on different biomedical datasets [19]. For example, in [20], unsupervised deep learning models discovered 32% of new relationships not originally known in the UMLS. In [21], recurrent neural networks (RNNs) and convolutional neural networks (CNNs) are fused to learn the features. RNNs and CNNs are combined for high-quality biomedical relationship extraction.

However, various associations between different datasets are likely to exist. For example, a gene in KEGG could be associated with a gene in PharmGKB. Since KEGG stores data in a different way than PharmGKB, it is time-consuming and arduous to combine the two databases directly. Overall, gene, drug, and disorder information has been stored in different heterogeneous datasets. These different datasets contain essential pieces of information for the identification of potential disorder biomarkers. Heterogeneity and fragmentation of these biomedical datasets make it challenging to quickly obtain essential information regarding particular genes, drugs, and disorders of interest. Furthermore, searching these enormous datasets and integrating the findings across the heterogeneous sources is costly and complicated [22]. Drug repositioning is one of the urgent issues that requires semantic relationship mining among genes, disorders, and drugs from different biomedical datasets for precision medicine.

Generally, these datasets provide query access for users through an application programming interface. Querying the relationships among genes, drugs, and disorders has become a research topic of increasing interest. The research on linked datasets capitalizes on the storage, management, and querying of information and promotes in-depth data analysis and data mining [23]. Semantic relationship mining among genes, disorders, and drugs is widely used, for example, in precision medicine and drug repositioning. For example, semantic relationships among diseases, drugs, genes, and variants are used to automatically identify potential drugs for precision medicine in the Precision Medicine Knowledgebase (PreMedKB) [24]. The semantic relationships between any two or more entities are queried to obtain comprehensive information. The semantic relationships among genes, disorders, drugs, and other concepts in a knowledge base can also be exploited for prioritizing drug repurposing or repositioning [25–27].
Drug repositioning is a relatively inexpensive and fast alternative to the lengthy and financially onerous task of new drug development [28]. Semantic relationship mining between a drug and other molecules or entities can also be used for drug-related knowledge discovery [29] and cooccurring entities analysis [30]. However, because these datasets could be stored in different places and in different ways, with different data formats and inconsistent representations of the same entity, the power of data mining across multiple datasets is far from being realized.

In this paper, a semantic relationship mining method among genes, disorders, and drugs from different biomedical datasets is presented. Semantic relationship mining across different biomedical datasets was performed to address this problem.

Parkinson’s disease (PD) is a pervasive neurodegenerative disorder that affects approximately 6 million people worldwide. Genes play an essential role in the development of PD. Monogenic forms account for approximately 10% of all PD cases [31], while the other cases are multifactorial. An increasing number of PD loci have been identified [32]. We used PD as a case study and focused on mining the putative and most current disorder-gene-drug relationships of PD from four different biomedical datasets. We addressed some of the current challenges in the field, such as integration with different existing medical datasets and the exploitation of semantic relationship mining in real-case scenarios. This approach transcends the limitations of distributed heterogeneous data sources and results in more complete datasets in such a way that medical researchers can freely access multiple datasets across platforms. This study will impact future translational medical research.

**Methods**

**Multisource data integration**

The following life science datasets were studied in this paper: SemMedDB, KEGG, Uniprot, and PharmGKB. Different organizations publish these datasets. UMLS Metathesaurus was introduced to solve the morphology and polysemy problems. These datasets contain domain patterns for disorders (disorder), chemicals and drugs (drug) and genes and molecular sequences (gene). Figure 1 shows nine drug-disorder, gene-disorder, and drug-gene relationships.

Before mining, we converted the relational databases (including PharmGKB, KEGG, Uniprot, and SemMedDB) into the RDF data format using the D2R tool [33] to obtain the SemMedRDF, KEGGRDF, UniprotRDF and PharmGKB RDF datasets. We constructed Algorithm I to mine the semantic relationship types between SemMedRDF and other life science linked open data datasets.

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**Fig. 1** Gene-Disorder-Drug Relationships

```
PRG1={R1, R2, R11, R13, R14, R22, R23}
PRG2={R1, R2, R3, R13, R14, R15, R21}
PRG3={R3, R6, R8, R13, R16, R19}
PRG4={R1, R2, R13, R14, R15, R22}
PRG5={R2, R13, R14, R15}
PRG6={R13, R21}
PRG7={R1, R2, R5, R6, R7, R13, R18, R19, R20}
PRG8={R3, R4, R13, R17, R25}
PRG9={R8, R12, R13}
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Algorithm 1: Multi-Source Semantic Integration

1. Let \( \Sigma = \text{SemMedRDF}, \text{KEGG RDF}, \text{UniProt RDF}, \text{PharmGKB RDF} \)
\
\( \text{DOJLinks} = \varnothing, \text{AllPreds} = \varnothing \).
2. Initializations: variables for the UMLS label, semMedRDF, UniProt RDF, PharmGKB RDF.
   \( \text{DOJLinks} = \varnothing, \text{AllPreds} = \varnothing \).
3. \( \text{For each predicate in the Metathesaurus of UMLS} \)
   \( \text{Add mapping to AllPreds and mark it with the CUI found in the} \)
   \( \text{Metathesaurus of UMLS} \).
   \( \text{Index AllPreds by predicate.} \)
   \( \text{All of the objects are replaced with itsclass-UMLS-rdf while} \)
   \( \text{getTriples(n, a, SemMedRDF; drug) \& getTriples(n, a, KEGG RDF)} \).
   \( \text{getTriples(n, a, KEGG RDF; gene) \& getTriples(n, a, PharmGKB RDF)} \).
   \( \text{getTriples(n, a, KEGG RDF; drug) \& getTriples(n, a, PharmGKB RDF)} \).
   \( \text{getTriples(n, a, KEGG RDF; gene) \& getTriples(n, a, PharmGKB RDF)} \).
   \( \text{getTriples(n, a, KEGG RDF; drug) \& getTriples(n, a, PharmGKB RDF)} \).
   \( \text{AllPreds is indexed on predicate.} \)
   \( \text{The first pred of AllPreds is obtained.} \)
   \( \text{If any two triples have the same CUI of the subject, predicate,} \)
   \( \text{and object while the namespace of the subject or object is different,} \)
   \( \text{this predicate will be one of the Links.} \)
   \( \text{All of the Links will be added to BMRDFs. It will link} \)
   \( \text{SemMedRDF to other biomedical datasets.} \)

Gene-disorder-drug semantic relationship mining

**Algorithm II: Semantic Relationship Mining among Genes, Drugs, and Disorders.**

Requirements: Gene, Drug, Disorder is the set of all entities that belong to the gene, drug, and disorder groups. Relation\_gene2disorder is the set of relationships between genes and disorders. Relation\_gene2drug is the set of relationships between genes and drugs, and so on.

1. For each entity g in Gene
2. For each g. neighborEntity
3. e = g.neighborEntity
4. p = g. predication(e) // get the predication p: (g, p, e)
5. If (e \( \in \) Gene)
6. Relation\_gene2gene.add(p)
7. EndIf
8. If (e \( \in \) Drug)
9. Relation\_gene2drug.add(p)
10. EndIf
11. If (e \( \in \) Disorder)
12. Relation\_gene2disorder.add(p)
13. EndIf
14. EndFor
15. EndFor
16. // the same steps for each entity in Drug and Disorder
To fully understand the relationships among genes, disorders, and drugs, the following algorithm was designed to mine the attribute relationships among the three.

In Algorithm II, three entity sets are defined first: Gene, Drug, and Disorder. The relationships are defined among the three: the relational dataset from gene to disorder is called Relation_gene2disorder; the relational dataset from a gene to a drug is called Relation_gene2drug; other relational datasets can be named similarly. The algorithm to accomplish relationship querying is described as follows:

1. Traverse every entity in the Gene dataset;
2. Traverse the adjacent entity e of each entity and the predicate relationship p between the two;
3. If the adjacent entity e belongs to the element of Gene dataset, add the relationship p to Relation_gene2gene; if it belongs to the Drug dataset, add the relationship p to Relation_gene2drug; if it belongs to Disorder dataset, add the relationship p to Relation_gene2disorder.

Traverse each entity in the Drug and Disorder datasets to obtain the corresponding relational dataset.

**Query pattern design**
Nine types of relational query patterns were designed based on the gene-drug-disorder relationships in Fig. 1.

| Table 1 Query patterns |
|------------------------|
| **No.** | **Query pattern** |
| Q1 | Query all genes related to a specific gene |
| Q2 | Query all disorders caused by a specific gene |
| Q3 | Query all drugs targeting a specific gene |
| Q4 | Query all disorders related to a specific disorder |
| Q5 | Query all genes causing a specific disorder |
| Q6 | Query all drugs treating a specific disorder |
| Q7 | Query all drugs related to a specific drug |
| Q8 | Query all disorders treated by a specific drug |
| Q9 | Query all genes targeted by a specific drug |
These query patterns are used in many research fields [25, 26, 34]. They are shown in Table 1.

It is necessary to know the possible paths from a disorder to a drug to query the relevant drugs for a particular disorder, as shown in the relationship path in Fig. 1. For example, the algorithm designed for querying all drugs that treat a specific disorder is shown in Algorithm III. The remaining query processes can be performed in the same manner.

**Algorithm III** - Query all drugs that treat a specific disorder.

**Require**: $S$ is the set of URIs of a disorder. Temp is the set of possible results.

1. For each triple $t$ matches (?s, myprop:UMLS-Label, disorder)
2. $S$.add(getSubject())
3. End for
4. For each URI $s$ in $S$
5. For each predicate $p$ in PRG6
6. For each triple $t$ matches ($s$, $p$, $?o$)
7. If(myclass:UMLS-Drug.contains(??o))
8. Temp.add(getObject())
9. EndIf
10. EndFor
11. EndFor
12. EndFor
13. return Temp

The algorithm to query all drugs that treat a specific disorder is described as follows:

Take the disorder name entered by the user as the object, and use the customized myprop: Label as the predicate to find the subject URI set $S$;

The relational set from disorder to drug analyzed in the previous section is the following: Traverse each URI in set $S$, and use each element in as predicate to query. The object set of the query is Temp;

Traverse Temp to remove the elements that are not in myclass: Drug;

Output the remaining results in Temp.

Other algorithms for related queries are similar, except that the relational set changes.

**Experiments and results**

**Experiment dataset**

Overall, any biomedical datasets can be used to mine the semantic relationships among them. SemMedDB, KEGG, Uniprot, and PharmGKB were used in the experiment.

**Semantic relationship mining results**

As shown in Table 2, 25 new relationships between the gene, disorder, and drug were mined from the SemMedRDF, KEGGRDF, UniprotRDF, and PharmGKB datasets. As there are many relationships, the relationships in Fig. 1 were replaced by numbers, and each relationship set is represented by nine predicate relationship groups (PRG1-PRG9) in Table 3. For example, in row 2 of Table 3, the new relationships R1, R2, R11, R13, R14, R22, and R23 belong to PRG1. These relationships are also associated with the query patterns Q1. The new relationships can help us to mine more semantic relationships.

**Query results**

1. Q1: Query all of the genes that are related to a specific gene, PARK2. There were 95 results (genes,
proteins, and molecular sequences) related to PARK2, including PARK7, GCH1, PACRG, FBXW8, PINK1, and NBR1 (Table 4). Among them, 61 results were from SemMedDB, 23 results belonged to PharmGKB, and 11 results were from Uniprot.

2. Q2: Query all of the disorders caused by a specific gene, PARK2. There were 123 results (disorders) caused by PARK2. Some results were autosomal recessive juvenile Parkinson disease, leukemia, chronic myeloid leukemia, carcinoma of the large intestine, chronic obstructive airway disease, and chromosomal translocation. SemMedDB yielded 81 results, and another 42 results belonged to PharmGKB.

3. Q3: Query all drugs that target a specific gene, PARK2. There were 68 results that target PARK2. Some results were Cholesterol, multicatalytic endopeptidase complex, ubiquitin-protein ligase, FBXW8, and Reactive Oxygen Species. SemMedDB yielded 55 results, and another 13 results belonged to PharmGKB.

4. Q4: Query all disorders involved in a specific disorder, Parkinson's. There were 66 results (disorders) involved in Parkinson's. Some results were encephalitis, tremor, depressive disorder, hypokinesia, cognitive deficit, respiratory failure, equilibration disorder, and Lewy body disease. All of the results belonged to SemMedDB.

5. Q5: Query all of the genes that cause a specific disorder, Parkinson's. There were 28 results (Genes, protein, and molecular sequences) involved in Parkinson's. Some results were PARK1, PARK2, and CHCHD2. PharmGKB yielded 25 results, and another 3 results belonged to SemMedDB.

6. Q6: Query all of the drugs that treat a specific disorder, Parkinson's. There were 79 results (Chemicals & Drugs) involved in Parkinson's. Some results were dopamine, levodopa, dopamine transporter, and multicatalytic endopeptidase complex. SemMedDB yielded 40 results, and another 11 results belonged to PharmGKB.

7. Q7: Query all of the drugs involved in a specific drug, Levodopa. There were 79 results involved in Levodopa. Some results were Reserpine, Acetylcholine, Antipsychotic Agents, Monoamine Oxidase, Serotonin, and Isoproterenol. SemMedDB yielded 67 results, and another 12 results were from KEGG.

8. Q8: Query all of the disorders treated by a specific drug, Levodopa. There were 47 results (disorders) involved in Levodopa. Some results are Parkinson's Disease, Seborrheic dermatitis, Hepatic Encephalopathy, Hepatic Coma, Hypotension, Secondary hyperprolactinemia due to prolactin-secreting tumor, Striatal Degeneration, nervous system disorder, and Hypokinesia.

| No. | Predictate | Object |
|-----|------------|--------|
| 1   | http://www4.wiwiss.fu-berlin.de/semdb/PREDICATE#COEXISTS_WITH | http://www4.wiwiss.fu-berlin.de/semdb/OBJECT_NAME#PARK7 |
| 2   | http://www4.wiwiss.fu-berlin.de/semdb/PREDICATE#COEXISTS_WITH | http://www4.wiwiss.fu-berlin.de/semdb/OBJECT_NAME#GCH1 |
| 3   | http://www4.wiwiss.fu-berlin.de/semdb/PREDICATE#COEXISTS_WITH | http://www4.wiwiss.fu-berlin.de/semdb/OBJECT_NAME#PACRGgene|PACRG |
| 4   | http://www4.wiwiss.fu-berlin.de/semdb/PREDICATE#COEXISTS_WITH | http://www4.wiwiss.fu-berlin.de/semdb/OBJECT_NAME#FBXW8 |
| 5   | http://www4.wiwiss.fu-berlin.de/pharmgkb/ASSOCIATION#ASSOCIATED | http://www4.wiwiss.fu-berlin.de/pharmgkb/Entity2_NAME#PINK1 |
| ... | ...        | ...    |
| 95  | http://www4.wiwiss.fu-berlin.de/uniprot/EXTERNALLINK | http://www4.wiwiss.fu-berlin.de/uniprot#NBR1 |
SemMedDB yielded 36 results, and another 11 results belonged to PharmGKB.

9. Q9: Query all of the genes that are targeted by a specific drug, Levodopa. There were 26 results (Genes, protein, and molecular sequences) involved in Levodopa. Some results were PARK1, PARK2, and CHCHD2. All of the results belonged to SemMedDB.

For the nine relationships between genes, disorders, and drugs, nine queries (Q1-Q9) were designed. Tables 5 and 6 record the source and respective proportions of each query result. To evaluate the results to improve the accuracy, we invited three professionals as domain experts to evaluate the query results. Two of these experts evaluated the results independently. The three experts provided their confidence levels (“Yes,” or “No”) in the query results. Each query result received the label “the correct query result” if it received more than two “Yes”. Otherwise, it was labeled “a false query result”. The analysis of the query results is shown in Tables 5 and 6: the column of “No” represents the nine queries. In the column of “(The number of correct query results): (The number of queries results)”, for example, in Table 4, “48: 56” means that there were 56 query results from SemMedDB for Q1 in total. Forty-eight of them received the “correct results” label. The column “Precision” means that the “The number of correct query results” out of the total “The number of query results.” For example, in Table 4, “91.11” means that the “The number of correct query results” of Q1 was 91.11% (82/90).

In Tables 5 and 6, the results are mainly from SemMedDB and PharmGKB. Furthermore, some of the results are from KEGG and Uniprot. The precision of PharmGKB, KEGG, and Uniprot was 100%. The precision of SemMedDB using the method in the paper published in the ISWC SEPDA 2019 workshop [35] was 83.08% (329: 396). The precision of SemMedDB using the method in this paper was 86.44% (376: 435), which was an increase of 4.04%.

The precision of the method published in the ISWC SEPDA 2019 workshop [35] was 87.68% (477/544). The precision of the method presented in this paper was 89.88% (524/583). The precision increased by 2.51%. Furthermore, the number of query results increased by 7.7% ((583–544)/583), and the number of correct query results increased by 9.5% ((524–477)/524). That means that the method in this paper can help mine more results with increased precision.

Discussion

Strengths

It is crucial to integrate SemMedDB with other databases in this method. SemMedDB is a database of semantic predictions (subject-predicate-object triples) from MEDLINE citations (titles and abstracts). SemMedDB currently contains approximately 98 million predictions from all PubMed citations (approximately 29.1 million citations, processed using MEDLINE BASELINE 2019) [8]. Over 3000 papers are added to MEDLINE every day. Therefore, new semantic relationships are added continuously to SemMedDB. The latest relationships can help to discover new relationships for related research. Some potential recommended drugs reported in the recent literature for PD have been found in the preliminary step work on drug repositioning based on this method.

In this paper, the semantic relationship mining method is used to explore interesting, hidden, or previously unknown biomedical relationships. Twenty-five new relationships are extracted in the verification experiment. It helps to improve the results with quantity and quality. Furthermore, interesting, hidden, or previously unknown biomedical relationships can help to detect the potential relationships between drugs and diseases [20, 36].

Table 5 Analysis of the query results from [35]

| No. | (The number of correct query results): (The number of query results) | Precision (%) |
|-----|---------------------------------------------------------------------|---------------|
|     | SemMedDB | PharmGKB | KEGG | Uniprot | Total |               |
| Q1  | 48: 56   | 23: 23   | –    | 11:11   | 82: 90 | 91.11        |
| Q2  | 56: 73   | 42: 42   | –    | –       | 98:115 | 85.22        |
| Q3  | 44: 52   | 13:13    | –    | –       | 57: 65 | 87.69        |
| Q4  | 54: 63   | –        | –    | –       | 54: 63 | 85.71        |
| Q5  | –        | 25: 25   | –    | –       | 25: 25 | 100          |
| Q6  | 29: 36   | 11:11    | –    | –       | 40: 47 | 85.11        |
| Q7  | 54: 61   | –        | 12:12| –       | 66: 73 | 90.41        |
| Q8  | 25: 32   | 11:11    | –    | –       | 36: 43 | 83.12        |
| Q9  | 19: 23   | –        | –    | –       | 19: 23 | 82.61        |
| Total | 329: 396 | 125: 125 | 12:12| 11:11   | 477: 544 | 87.68        |
The nine types of common query patterns are proposed in the baseline method. This approach covers all semantic relationships between genes, disorders and drugs. Compared with the other models, our method can be extended to be used in more applications without a training dataset. Moreover, the method can also meet the requirements of processing large-scale data without high computational cost. The processing time increases with the size of the data linearly. It is more effective than the machine learning method, such as SemRep. In SemMedDB, the weighted average precision of the predictions is based on the number of predictions evaluated, which was approximately 0.79 [37–40]. In this paper, we used the approach in [34] to extract high-quality triples from SemMedDB. The precision increased by 2.27%.

Limitations and future effort
Since the fact that the quality of the datasets will affect the semantic relationship mining, the method has some limitations: (1) The quality of the SemMedDB should be improved in future research. (2) The quality of the other datasets depends on their creators. Thus, high-quality datasets will be selected carefully. Alternatively, we will try our best to improve the quality of the datasets selected. (3) Currently, mining semantic relationships among genes, disorders, and drugs from different biomedical datasets is the first step for precision medicine and drug repositioning. It would be desirable to mine repositioning drugs based on semantic relationships for more disorders, such as PD, Alzheimer’s Disease, cancer.

Conclusions
In this paper, a semantic relationship mining method among genes, disorders, and drugs was developed. In this method, data from various biomedical datasets were first converted into RDF triples and then integrated into a system for querying nine types of common query patterns. We focused on mining the putative and latest gene-disorder-drug relationships about PD. The experiment was conducted on four different datasets. The results showed that our method has significant advantages in integrating multisource heterogeneous biomedical data. Twenty-five new relationships among genes, disorder, and drugs were identified, and most of them came from different datasets. Moreover, the precision of our method increased by 2.51%. The number of query results increased by 7.7%, and the number of correct queries increased by 9.5%. These findings demonstrate that our method is robust and reliable in mining important gene-disorder-drug relationships.

Abbreviations
CUI: Concept unique identifier; KEGG: the Kyoto Encyclopedia of Genes and Genomes; PD: Parkinson’s disease; RDF: Resource description framework; SemMedDB: Semantic MEDLINE Database; URI: Uniform resource identifier

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The content is solely the responsibility of the authors.

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Authors’ contributions
LZ and GR designed the study and drafted the original manuscript. JH and QX collected the data and performed the experiments. FL revised the manuscript. GR and CT supervised the study. All authors have read and approved the manuscript.

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Table 6 Analysis of the query results from this paper

| No. | SemMedDB | PharmGKB | KEGG | Uniprot | Total | Precision (%) |
|-----|----------|----------|------|---------|-------|---------------|
| Q1  | 53: 61   | 23: 23   | –    | 11:11   | 87: 95| 91.58         |
| Q2  | 67: 81   | 42: 42   | –    | –       | 109: 123| 88.62         |
| Q3  | 48: 55   | 13: 13   | –    | –       | 61: 68| 89.71         |
| Q4  | 58: 66   | –        | –    | –       | 58: 66| 87.88         |
| Q5  | 2: 3     | 25: 25   | –    | –       | 27: 28| 96.43         |
| Q6  | 34: 40   | 11: 11   | –    | –       | 45: 51| 88.24         |
| Q7  | 60: 67   | –        | 12: 12| –       | 72: 79| 91.14         |
| Q8  | 31: 36   | 11: 11   | –    | –       | 42: 47| 89.36         |
| Q9  | 23: 26   | –        | –    | –       | 23: 26| 88.46         |
| Total | 376: 435 | 125: 125 | 12: 12| 11: 11 | 524: 583| 89.88         |
Availability of data and materials
The PharmGKB is available at https://www.pharmgkb.org. The UniProt is available at https://www.uniprot.org. The KEGG is available at https://www.genome.jp/kegg. The SemMedDB is available at https://skr3.nlm.nih.gov/SemMedDB. The query results are available from the corresponding author upon request.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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