Extracting drug-drug interactions from pharmacological texts.

Isabel Segura Bedmar, Cesar de Pablo-Sánchez, (joint work with Mario Crespo and Paloma Martínez)

CS Department, Universidad Carlos III de Madrid

September 2009
Saarbrücken, Germany
U. Carlos III de Madrid

http://www.uc3m.es/

Founded on 1989

3 campus in Madrid province

Getafe (Humanities, Social Sciences)
Leganés (Engineering)
Colmenarejo
Research on LT

– IE on pharmacological and clinical domain
– Question Answering
– Natural Interaction in real environments
  • E-commerce
  • People with disabilities
• 6 Madrid research group (30 doctors) UNED, UAM, UC3M, UEM, UPM and CINDOC

• Network of companies and research groups academic vs. professional research vs. services resource generation vs. applications
Human Language Technologies:
Distributed, Multilingual & Multimedia Information Retrieval
Automatic Question & Answer Systems with Natural Language
Semantic Web
Automatic Document Classification and Document Summarization
Representation and Extraction of Linguistic Information

Scientific Communication via WWW:
Cybermetric indicators, Webometrics
Cultural, scientific, technical and business web sites
Digital Libraries
User-centered design: usability, accessibility and visualization
Extracting drug-drug interactions from pharmacological texts.

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What is a Drug-Drug Interaction?
Beneficial

Ritonavir + Lopinavir = Effective antiretroviral
Nifedipine + propranolol = Antianginal drug
Dangerous

Aspirin + Heparin → Bleeding
Aspirin + Acetazolamide → Death
Medication errors kill 7,000 patients per annum in USA\textsuperscript{1}.

5% of medication errors are DDI\textsuperscript{2}.

High incidence in certain patient groups.

Increase the Healthcare costs

Kohn et al., 2000. “To Err is Human”.
Leape et al., 1995. “Systems analysis of adverse drug events”.
Drug interaction Resources

Most effective source: Medical Literature.
How Information Extraction helps?

**Aspirin** may decrease the effects of probenecid, sulfinpyrazone, and phenylbutazone.

\[ DDI \text{ may decrease ( Aspirin, Probenecid) } \]
\[ DDI \text{ may decrease ( Aspirin, Sulfinpyrazone) } \]
\[ DDI \text{ may decrease ( Aspirin, Phenylbutazone) } \]
What will you see in this talk?

Construction of an annotated corpus with DDI

Information Extraction System for DDI

- Text Analysis
- Drug Name Recognition
- Anaphora Resolution
- DDI Extraction
DrugBank is supported by David Wishart, Departments of Computing Science & Biological Sciences, University of Alberta.
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand Mixtures</td>
<td>Not Available</td>
</tr>
<tr>
<td>Chemical IUPAC Name</td>
<td>6-[5-acetamido-4,6-dihydroxy-2-(sulfooxy)oxan-3-yl]oxy-3-[5-(6-carboxy-4,5-dihydroxy-3-sulfooxy)oxan-2-yl]oxy-6-(hydroxymethyl)-3-(sulfoamino)-4-sulfooxyoxan-2-yl]oxy-4-hydroxy-5-sulfooxyoxane-2-carboxylic acid</td>
</tr>
<tr>
<td>Chemical Formula</td>
<td>C_{26}H_{42}N_{2}O_{37}S_{5}</td>
</tr>
<tr>
<td>Chemical Structure</td>
<td>![Chemical Structure Image]</td>
</tr>
<tr>
<td>CAS Registry Number</td>
<td>9005-49-6</td>
</tr>
<tr>
<td>InChI Identifier</td>
<td>InChI=1/C26H42N2O37S5/c1-4(30)27-7-9(31)13(6(56-23(1339)3-55-67(43,44,45)58-26-19(65-70(52,53)54)12(34)16(20(62-26)22(37)38)60-248(151-20,23-26,28-29,31-34,39H,2-3H2,1H3,(H,27,30)(H,35,36)(H,37,38)(H,40,41,42)(H,43,44,45)(H,46,47,48)(H,49,50,51)9(H,52,53,54)1/1h27,35,37,40,43,46,49,52H</td>
</tr>
<tr>
<td>InChI Key</td>
<td>HTTJABKRGRZYN-KXAJDVGVCI</td>
</tr>
<tr>
<td>KEGG Drug</td>
<td>Not Available</td>
</tr>
</tbody>
</table>
Showing Interaction Insert for Heparin

Drug Interactions:

a. Drugs Enhancing Heparin Effect:
Oral anticoagulants: Heparin sodium may prolong the one-stage prothrombin time. Therefore, when heparin sodium is given with dicumarol or warfarin sodium, a period of at least 5 hours after the last intravenous dose or 24 hours after the last subcutaneous dose should elapse before blood is drawn if a valid prothrombin time is to be obtained.

Platelet inhibitors: Drugs such as acetylsalicylic acid, dextran, phenylbutazone, ibuprofen, indomethacin, dipyriramole, hydroxychloroquine and others that interfere with platelet-aggregation reactions (the main hemostatic defense of heparinized patients) may induce bleeding and should be used with caution in patients receiving heparin sodium.

The anticoagulant effect of heparin is enhanced by concurrent treatment with antithrombin III (human) in patients with hereditary antithrombin III deficiency. Thus in order to avoid bleeding, reduced dosage of heparin is recommended during treatment with antithrombin III (human).

b. Drugs Decreasing Heparin Effect:
Digitalis, tetracyclines, nicotine, or antihistamines may partially counteract the anticoagulant action of heparin sodium. Heparin Sodium injection should not be mixed with doxorubicin, droperidol, ciprofloxacin, or mitoxantrone, since it has been reported that these drugs are incompatible with heparin and a precipitate may form.

Drug Interactions - Termino
Collecting a corpus for DDI
# Annotation of Corpus DrugDDI

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Avg. per doc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documents</td>
<td>579</td>
<td></td>
</tr>
<tr>
<td>Sentences</td>
<td>5806</td>
<td>10.2</td>
</tr>
<tr>
<td>Sentences with at least one DDI</td>
<td>2044</td>
<td>3.5</td>
</tr>
<tr>
<td>Drugs</td>
<td>14930</td>
<td>25.7</td>
</tr>
<tr>
<td>Drug-Drug Interactions</td>
<td>3027</td>
<td>5.2</td>
</tr>
</tbody>
</table>
Example of annotation

- `<SENTENCES>`
  - `<SENTENCE ID="s0" TEXT="Uricosuric Agents: Aspirin may decrease the effects of probenecid, sulfinpyrazone, and phenylbutazone."/>`
  + `<PHRASES>`</PHRASES>`
  - `<DDIS>`
    - `<DDI ID="s0.dd1" ID_1="s0.p2" ID_2="s0.p6" DRUG_1="Aspirin" DRUG_2="probenecid"/>
    - `<DDI ID="s0.dd2" ID_1="s0.p2" ID_2="s0.p7" DRUG_1="Aspirin" DRUG_2="sulfinpyrazone"/>
    - `<DDI ID="s0.dd3" ID_1="s0.p2" ID_2="s0.p9" DRUG_1="Aspirin" DRUG_2="phenylbutazone"/>
  </DDIS>`
</SENTENCE>
+ `<SENTENCE ID="s1" TEXT="Alcohol: Has a synergistic effect with aspirin in causing gastrointestinal bleeding."/>
+ `<SENTENCE ID="s2" TEXT="Corticosteroids: Concomitant administration with aspirin may increase the risk of gastrointestinal ulceration and may reduce serum salicylate levels."/>
+ `<SENTENCE ID="s3" TEXT="Pyrazolone Derivatives (phenylbutazone, oxyphenbutazone, and possibly dipyrone): Concomitant administration with aspirin may increase the risk of gastrointestinal ulceration."/>
+ `<SENTENCE ID="s4" TEXT="Nonsteroidal Antiinflammatory Agents: Aspirin is contraindicated in patients who are hypersensitive to nonsteroidal anti-inflammatory agents."/>
+ `<SENTENCE ID="s5" TEXT="Urinary Alkalinizers: Decrease aspirin effectiveness by increasing the rate of salicylate renal excretion."/>
</SENTENCE>`
What will you see in this talk?

Construction an annotated corpus with DDI

Information Extraction System for DDI

Text Analysis

Drug Name Recognition

Anaphora Resolution

DDI Extraction
IE System for DDI

Corpus TXT

Biomedical Resources

Text analysis

Drug Name Recognition

Anaphora Resolution

DDI Extraction

XML annotated with shallow syntactic and semantic information

+ drugs and other biomedical concepts

+ anaphoras

+ Drug interactions
IE System for DDI

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Biomedical Resources
Text Analysis by UMLS MetaMap program (MMTx)

Corpus TXT

Unified Medical Language System (UMLS)

UMLS MetaMap (MMTx): Text analysis

XML annotated with shallow syntactic and semantic information from UMLS
Sentence Splitting

- `<SENTENCES>`
  + `<SENTENCE ID="s0" TEXT="Uricosuric Agents: Aspirin may decrease the effects of probenecid, sulfinpyrazone, and phenylbutazone."/>
  </SENTENCE>
  + `<SENTENCE ID="s1" TEXT="Alcohol: Has a synergistic effect with aspirin in causing gastrointestinal bleeding."/>
  </SENTENCE>
  + `<SENTENCE ID="s2" TEXT="Corticosteroids: Concomitant administration with aspirin may increase the risk of gastrointestinal ulceration and may reduce serum salicylate levels."/>
  </SENTENCE>
  + `<SENTENCE ID="s3" TEXT="Pyrazolone Derivatives (phenylbutazone, oxyphenbutazone, and possibly dipyrone): Concomitant administration with aspirin may increase the risk of gastrointestinal ulceration."/>
  </SENTENCE>
  + `<SENTENCE ID="s4" TEXT="Nonsteroidal Antiinflammatory Agents: Aspirin is contraindicated in patients who are hypersensitive to nonsteroidal anti-inflammatory agents."/>
  </SENTENCE>
  + `<SENTENCE ID="s5" TEXT="Urinary Alkalizers: Decrease aspirin effectiveness by increasing the rate of salicylate renal excretion."/>
  </SENTENCE>
  + `<SENTENCE ID="s6" TEXT="Phenobarbital: Decreases aspirin effectiveness by enzyme induction."/>
  </SENTENCE>
  + `<SENTENCE ID="s7" TEXT="Phenytoin: Serum phenytoin levels may be increased by aspirin."/>
  </SENTENCE>
  + `<SENTENCE ID="s8" TEXT="Propranolol: May decrease aspirin's anti-inflammatory action by competing for the same receptors."/>
  </SENTENCE>
  + `<SENTENCE ID="s9" TEXT="Antacids: Enteric Coated Aspirin should not be given concurrently with antacids, since an increase in the pH of the stomach may effect the enteric coating of the tablets."/>
  </SENTENCE>`
Shallow Syntactic Information

- <SENTENCES>
  - <SENTENCE ID="s0" TEXT="Uricosuric Agents: Aspirin may decrease the effects of probenecid, sulfinpyrazone, and phenylbutazone.">
    - <PHRASES>
      + <PHRASE ID="s0.p0" NUMTOKENS="2" TEXT="Uricosuric Agents" TYPE="NP"></PHRASE>
      + <PHRASE ID="s0.p1" NUMTOKENS="1" TEXT="" TYPE="UNK" USAN="NO"></PHRASE>
      + <PHRASE ID="s0.p2" NUMTOKENS="1" TEXT="Aspirin" TYPE="NP"></PHRASE>
      + <PHRASE ID="s0.p3" NUMTOKENS="1" TEXT="may" TYPE="VP"></PHRASE>
      + <PHRASE ID="s0.p4" NUMTOKENS="1" TEXT="decrease" TYPE="VP"></PHRASE>
      + <PHRASE ID="s0.p5" NUMTOKENS="2" TEXT="the effects" TYPE="NP"></PHRASE>
      + <PHRASE ID="s0.p6" NUMTOKENS="3" TEXT="of probenecid" TYPE="PP/of"></PHRASE>
      + <PHRASE ID="s0.p7" NUMTOKENS="2" TEXT="sulfinpyrazone" TYPE="NP"></PHRASE>
      + <PHRASE ID="s0.p8" NUMTOKENS="1" TEXT="and" TYPE="CONJ"></PHRASE>
      + <PHRASE ID="s0.p9" NUMTOKENS="2" TEXT="phenylbutazone" TYPE="NP"></PHRASE>
    </PHRASES>
  </SENTENCE>
</SENTENCES>
Uricosuric Agents: Aspirin may decrease the effects of probenecid, sulfinpyrazone, and phenylbutazone.
Uricosuric Agents: Aspirin may decrease the effects of probenecid, sulfinpyrazone, and phenylbutazone.
**Drug Name Recognition**

- **Corpus TXT**
- **UMLS**
- **WHOINN affixes**

**Text analysis**
- **Drug Name Recognition**
- **Anaphora Resolution**
- **DDI Extraction**

Output:
- XML annotated with shallow syntactic and semantic information
- Drugs and other biomedical concepts
- Anaphoras
- Drug interactions
Is MMTx enough to recognize Drugs?

<table>
<thead>
<tr>
<th>New Drugs</th>
<th>Date of Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valturna (aliskiren and valsartan) Tablets</td>
<td>September 17, 2009</td>
</tr>
<tr>
<td>Influenza A (H1N1) 2009 Monovalent Vaccine</td>
<td>September 15, 2009</td>
</tr>
<tr>
<td>Zirgan (ganciclovir) Ophthalmic Gel</td>
<td>September 15, 2009</td>
</tr>
<tr>
<td>Vibativ (telavancin) Injection</td>
<td>September 11, 2009</td>
</tr>
<tr>
<td>Bepreve (bepotastine) Ophthalmic Solution</td>
<td>September 8, 2009</td>
</tr>
<tr>
<td>Metozolv ODT Orally Disintegrating Tablets</td>
<td>September 4, 2009</td>
</tr>
<tr>
<td>Intuniv (guanfacine) Extended Release Tablets</td>
<td>September 2, 2009</td>
</tr>
<tr>
<td>Zenpep (pancrelipase) Capsules</td>
<td>August 27, 2009</td>
</tr>
<tr>
<td>Sabril (vigabatrin) Tablets and Oral Solution</td>
<td>August 21, 2009</td>
</tr>
<tr>
<td>Hiberix Solution for Intramuscular Injection</td>
<td>August 19, 2009</td>
</tr>
<tr>
<td>Extavia (interferon beta-1b)</td>
<td>August 14, 2009</td>
</tr>
<tr>
<td>Saphris (asenapine) Sublingual Tablets</td>
<td>August 13, 2009</td>
</tr>
<tr>
<td>Embeda Extended Release Capsules</td>
<td>August 13, 2009</td>
</tr>
<tr>
<td>Livalo (pitavastatin) Tablets</td>
<td>August 3, 2009</td>
</tr>
</tbody>
</table>
Is MMTx enough to classify Drugs?

UMLS Semantic Types for drugs:

**Clinical Drug (clnd):** a pharmaceutical preparation as produced by the manufacturer.

**Pharmacological substance (phsu):** a substance used in the treatment or prevention of pathologic disorders.

**Antibiotic (antb):** A pharmacologically active compound produced by growing microorganisms which kill or inhibit growth of other microorganisms.
Affix-based classification obtains an accuracy rate of 75%
Drug name recognition and classification in biomedical texts (Segura-Bedmar et al., 2008)
Drug Anaphora Resolution

*Corpus TXT*

[Image 84x405 to 140x477]

*Drug Name Recognition*

[Image 242x71 to 482x482]

*Anaphora Resolution*

[Image 553x382 to 607x452]

*DDI Extraction*

[Image 553x278 to 621x362]

- XML annotated with shallow syntactic and semantic information
- drugs and other biomedical concepts
- anaphoras
- Drug interactions

*Biomedical Resources*
How Anaphora Resolution helps?

**Levofloxacin** is one of the most commonly prescribed antibiotics in clinical practice. Several case reports have indicated that **this drug** may significantly potentiate the anticoagulation effect of **warfarin**.

*DDI MAY POTENTIATE ( LEVOFLOXACIN, WARFARIN )*
Score-based approach for Anaphora Resolution in Drug-Drug Interacion Documents
(Segura-Bedmar et al., 2009a)
NLDB 2009

DrugNerAR: Linguistic Rule-Based Anaphora Resolution for DDI Extraction in pharmacological documents
(Segura-Bedmar et al., 2009b)
To appear in DTMBIO 2009
Anaphora Resolution in DDI Documents

Identification of anaphoric expressions

Selection of candidate antecedents

Ordering candidate antecedents
Scoring candidates

Pronominal

\[ Distance(Cand_i) = N \times \frac{d_{\text{max}} - d_i}{d_{\text{max}} - d_{\text{min}}} \]

Nominal

\[ \text{Morpho}(Cand_i) = N \times (1 - \frac{\text{min} - \text{LCS(anaphor, cand}_i) }{\text{min}}) \]
Since the concomitant administration of warfarin with amiodarone increases the prothrombin time by 100% after 3 to 4 days, the dose of the anticoagulant should be reduced by one-third to one-half, and prothrombin times should be monitored closely.
Since the concomitant administration of warfarin with amiodarone increases the prothrombin time by 100% after 3 to 4 days, the dose of the anticoagulant should be reduced by one-third to one-half, and prothrombin times should be monitored closely.
Quinidine and procainamide doses should be reduced by one-third when either is administered with amiodarone. Plasma levels of flecainide have been reported to increase in the presence of oral amiodarone; because of this, the dosage of flecainide should be adjusted when these drugs are administered concomitantly.
Anaphora resolution results
Drug-Drug Interaction Extraction

Corpus TXT

Text analysis

Drug Name Recognition

Anaphora Resolution

DDI Extraction

XML annotated with shallow syntactic and semantic information

+ drugs and other biomedical concepts

+ anaphoras

+ Drug interactions

Biomedical Resources
Approaches for DDI Detection

Syntactic Information and Pattern Matching.
Subsequence Kernel Method (Giuliano et al., 2006)
# Pharmacological patterns

Patterns defined by our pharmacist.

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>&lt;DRUG&gt;</code> INTERACT WITH <code>&lt;DRUG&gt;</code>.</td>
<td></td>
</tr>
<tr>
<td><code>&lt;DRUG&gt;</code> (INCREASE</td>
<td>DECREASE</td>
</tr>
<tr>
<td><code>&lt;DRUG&gt;</code> INTERFERE WITH <code>&lt;DRUG PROPERTIES&gt;</code></td>
<td></td>
</tr>
<tr>
<td>CONCURRENT USE OF <code>&lt;DRUG&gt;</code> WITH <code>&lt;DRUG&gt;</code> (INCREASE</td>
<td>DECREASE</td>
</tr>
<tr>
<td><code>&lt;DRUG&gt;</code> INHIBIT <code>&lt;DRUG PROPERTIES&gt;</code></td>
<td></td>
</tr>
<tr>
<td>CO-ADMINISTRATION OF <code>&lt;DRUG&gt;</code> AND <code>&lt;DRUG&gt;</code> RESULT IN <code>&lt;DRUG PROPERTIES&gt;</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;DRUG EFFECTS&gt;</code> OF <code>&lt;DRUG&gt;</code> BE (ENHANCED</td>
<td>REDUCED</td>
</tr>
</tbody>
</table>
How syntactic information helps?

Detecting appositive structures

The pressor effects of [catecholamines such as dopamine or norepinephrine]_APOS are enhanced by Bretylium Tosylate.

which can be interpreted as:

1) The pressor effects of catecholamines are enhanced by Bretylium
2) The pressor effects of dopamine are enhanced by Bretylium
3) The pressor effects of norepinephrine are enhanced by Bretylium

<DRUG EFFECT> OF (DRUG|APOS) BE <INTERACT_VERB> BY (DRUG|APOS)

1) DDI increase (BRETYLIUM TOSYLATE, CATECHOLAMINES)
2) DDI increase (BRETYLIUM TOSYLATE, DOPAMINE)
3) DDI increase (BRETYLIUM TOSYLATE, NOREPINEPHRINE)
How syntactic information helps?

Detecting coordinative propositions

Aspirin may interact with [probenecid, sulfinpyrazone, and phenylbutazone]_COORD

which can be interpreted as:
1) Aspirin may interact with probenecid
2) Aspirin may interact with sulfinpyrazone.
3) Aspirin may interact with phenylbutazone

(\textsc{drug}|\textsc{coord}) \textsc{interact with} (\textsc{drug}|\textsc{coord})

1) DDI \textsc{may interact} (ASPIRIN, PROBENECID)
2) DDI \textsc{may interact} (ASPIRIN, SULFINPYRAZONE)
3) DDI \textsc{may interact} (ASPIRIN, PHENYLBUTAZONE)
What is the problem?

Complex sentences: Interactions could span several clauses

[The Cmax of norethindrone was 13% higher] when [it was coadministered with gabapentin]

In a pharmacokinetic substudy in patients with congestive heart failure receiving furosemide or digoxin in whom therapy with FLOLAN was initiated, apparent oral clearance values for furosemide (n = 23) and digoxin (n = 30) were decreased by 13% and 15%, respectively, on the second day of therapy and had returned to baseline values by day 87.
How to improve the results?

DDI Extraction

Drug interactions

Syntactic Simplification and Pattern Matching. **Kernel Method for DDI Extraction.**
Concurrent administration of a **TNF antagonist** with **ORENCIA** has been associated with an increased risk of serious infections and no significant additional efficacy over use of the **TNF antagonists** alone.

**DDI**:

- DDI(TNF antagonist, ORENCIA)
- DDI(ORENCIA, TNF antagonist)
- DDI(TNF antagonist, TNF antagonist)

---

**ML and Kernel approach to DDI**

- Classification problem
- Every drug pair is an instance
- Relation is reciprocal, drug order is not important
- Unbalanced dataset: 10% positives
Shallow sequence kernels

Learning algorithm: SVM

Shallow representation of sentences (no syntax)

- Global Context Kernel: whole sentence info
  - Before - Between
  - Between
  - Between - After

- Local Context Kernel: entity info

\[ K_{SS}(A_1,A_2) = K_{GC}(A_1,A_2) + K_{LC}(A_1,A_2) \]

Claudio Giuliano, Alberto Lavelli, Lorenza Romano. Exploiting Shallow Linguistic Information for Relation Extraction from Biomedical Literature, EACL 2006
Concurrent administration of a TNF antagonist with ORENCIA has been associated with an increased risk of serious infections and no significant additional efficacy over use of the TNF antagonists alone.

\[ K_{GC(A_1,A_2)} = K_{FB(A_1,A_2)} \]
Global Context: Between

Concurrent administration of a **TNF antagonist with ORENCIA** has been associated with an increased risk of serious infections and no significant additional efficacy over use of the **TNF antagonists** alone.

\[ K_{GC}(A_1,A_2) = K_{FB}(A_1,A_2) + K_B(A_1,A_2) \]
Concurrent administration of a TNF antagonist with ORENCIA has been associated with an increased risk of serious infections and no significant additional efficacy over use of the TNF antagonists alone.

\[ K_{GC(A_1,A_2)} = K_{FB(A_1,A_2)} + K_{B(A_1,A_2)} + K_{BA(A_1,A_2)} \]
Concurrent administration of a TNF antagonist with ORENCIA has been associated with an increased risk of serious infections and no significant additional efficacy over use of the TNF antagonists alone.

\[
K_{GC}(A_1,A_2) = K_{FB}(A_1,A_2) + K_{B}(A_1,A_2) + K_{BA}(A_1,A_2)
\]

\[
\Phi_c(A_1) = \{ \text{concurrent administration of a } \text{TNF antagonist with ORENCIA} \}
\]
Concurrent administration of a **TNF antagonist** with ORENCIA has been associated with an increased risk of serious infections and no significant additional efficacy over use of the **TNF antagonists** alone.

\[ K_{LC}(A_1,A_2) = K_{LEFT}(A_1,A_2) + K_{RIGHT}(A_1,A_2) \]
Concurrent administration of a TNF antagonist with ORENCIA has been associated with an increased risk of serious infections and no significant additional efficacy over use of the TNF antagonists alone.

$$K_{LC}(A_1,A_2)=K_{LEFT}(A_1,A_2) + K_{RIGHT}(A_1,A_2)$$
Concurrent administration of a **TNF antagonist** with **ORENCIA** has been associated with an increased risk of serious infections and no significant additional efficacy over use of the **TNF antagonists** alone.

\[
K_{LC}(A_1,A_2) = K_{LEFT}(A_1,A_2) + K_{RIGHT}(A_1,A_2)
\]

\[
\Phi_c(A_1) = \{ \begin{array}{l}
\text{Token(of)}
\text{Lemma(of)}
\text{PoS(of)}
\text{Stem(of)}
\text{Ortho(of)}
\text{...}
\text{Token(with)}
\text{Lemma(with)}
\text{PoS(with)}
\text{Stem(with)}
\end{array} \}
\]
Comparative Patterns, Syntactic + Patterns, kernels
IE System for DDI

Corpus TXT

Text analysis

Drug Name Recognition

Anaphora Resolution

DDI Extraction

XML annotated with shallow syntactic and semantic information

+ drugs and other biomedical concepts

+ anaphoras

+ Drug interactions

Biomedical Resources
Drug Drug Interaction detection is a promising application for IE and NLP.