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Searching Haptens, Carrier Proteins, and Anti-hapten Antibodies

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Summary

Haptens are small molecules that are usually nonimmunogenic unless coupled to some carrier proteins. The generation of anti-hapten antibodies is important for the development of immunodiagnosics and therapeutics. Recently, our group has developed a database called HaptenDB, which provides comprehensive information about 1,087 haptens. In this chapter, we describe following web tools integrated in HaptenDB: (i) keyword search facility allows search on major fields, (ii) browsing service, to display all haptens, carrier proteins and antibodies, and (iii) structure similarity search, which allows the users to search their structure against hapten structures.

Key Words: Carrier protein, database, hapten, haptenDB, pesticides

1. Introduction

Haptens are small molecules, such as pesticides, drugs, hormones, and toxins, which are usually nonimmunogenic unless coupled with some macromolecules such as proteins. These carrier molecules provide T lymphocyte help required for the induction of humoral (antibody) response. Direct coupling of hapten with carrier protein is possible where the target compound contains functional groups such as $-NH_2$ and $-COOH$. Alternatively, these functional groups can be introduced by derivatization of the hapten. Thus, the production of anti-hapten antibodies of desired specificity depends on hapten design (preserving the chemical structure and spatial conformation of target compound), selection of appropriate carrier protein, and the conjugation method (*I*). Antibodies once

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01 generated can be exploited for multiple applications such as in serology, drug
02 delivery, and development of immunodiagnostic kits.

03 Most of the contaminants in the environment including soil, water, air, and
04 food are small molecules that are often nonimmunogenic (haptens). Moreover,
05 the haptens can be altered structurally to raise the antibodies of defined speci-
06 ficity and affinities toward target analyte. Immunochemical techniques such
07 as immunoassays, immunosensors, immunochromatography, and immunola-
08 beling supplement traditional analytical methods in an ideal way because
09 these are extremely sensitive, simple, and inexpensive. Standardized immuno-
10 chemical methods for medicine, food, and environmental monitoring calls for
11 the generation of antibodies of defined specificities and affinities against the
12 analyte/hapten.

13 Immunology has followed the trend of molecular biology in the explosive
14 generation of new data. The amount of data pertaining to haptens is overwhelm-
15 ingly increasing because of its growing applied importance. Advances in
16 database technology have enabled us to manage these data efficiently, while at
17 the same time, bioinformatics have provided new tools for data analysis. Though
18 there are number of immunological databases on protein sequences and peptides
19 (epitopes) (KABAT, IMGT, FIMM, MHCBN, BCIPEP, and AntiJen 2.0)
20 (2– 7), but there is only one database on haptens called HaptenDB (8).
21 HaptenDB is a comprehensive database comprising haptens, carrier molecules,
22 and the antibodies where the information has been collected from the web
23 sources and the standard literature (8). HaptenDB, the first of its kind, aims at
24 providing the information about chemical, physical, and structural properties
25 of haptens to the user . Besides, it also contains information about the carrier
26 molecules used to raise the antibodies against the particular hapten, together
27 with the conjugation methods, immunization schedules, host organism, and the
28 properties of the antibodies generated. The database further describes the assay
29 method, which could be used to characterize the antibody, as well as the appli-
30 cation of the antibody generated, e.g., in immunodiagnostics. The database is
31 comprehensive in itself as it has integrated many aspects of the hapten that
32 one would like to gather for research or application purpose. Furthermore,
33 the database has some structure similarity tools that would enable the user to
34 check against the query, whether the database has entries to similar/or related
35 structures and respective antibodies. To collect the particular information, if
36 not entered in the database, the reference and web link of each source is
37 given. Although the database is made user-friendly by making each page self-
38 explanatory, still one can go to Help, Information, and Related links options
39 on Home Page.

01 **2. Materials**02 **2.1. Web Server**

03 The HaptenDB web server was developed in a UNIX environment on SUN
 04 server420R in Solaris 7.0. This server is designed to provide easy access to the user,
 05 based on a set of simple graphical user interface (GUI) forms. Methods for
 06 searching the databases and displaying the selected objects were built with a
 07 combination of Java Scripts and CGI-scripts in PERL 5.4. One can access database
 08 and web tools via Internet from <http://www.imtech.res.in/raghava/haptendb/>
 09 or <http://www.imtech.ac.in/raghava/haptendb/>. In order to provide search
 10 on any field of database and to maintain standards, SRS version of
 11 HaptenDB (<http://www.imtech.res.in/srs/>) and its mirror sites have been launched
 12 on SGI origin server under IRIX environment, which is available from
 13 <http://bioinformatics.uams.edu/>.
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15 **2.2. Description of Data**

16
 17 The current version of the database has 2,021 entries for 1,087 haptens and
 18 25 carrier proteins. Each entry provides comprehensive details about (i) nature
 19 of the hapten, (ii) information about carrier protein, (iii) coupling method, (iv)
 20 methods of anti-hapten antibody production, (v) assay method (used for charac-
 21 terization), and (vi) specificities of antibodies. Moreover, the haptens and the
 22 antibodies are categorized on the basis of their nature, for example, pesticides,
 23 herbicides, insecticides, drugs, toxins, steroids, and hormones. Tables 1 and 2
 24 present the number of haptens and antibodies entered so far under different
 25 categories.
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28 **Table 1**
 29 **Distribution of haptens (1,087)**

30 Category	Number of entries
31 Pesticides, insecticides, fungicides, herbicides, etc.	225
32 Toxins	26
33 Drugs, antibiotics, analgesics, narcotics, etc.	120
34 Hormones, auxins, phytoestrogens, etc.	19
35 Synthetic and natural peptides	17
36 Vitamins and their analogs	18
37 Others (dyes, explosives, etc.)	99
38 Unclassified haptens or haptens belonging to smaller groups	563
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Table 2
Distribution of anti-hapten antibodies entries (2,021)

Category	Number of entries
Pesticides, insecticides, fungicides, herbicides, etc.	650
Toxins	40
Drugs, antibiotics, analgesics, narcotics, etc.	200
Hormones, auxins, phytoestrogens, etc.	30
Synthetic and natural peptides	41
Vitamins and their analogs	50
Others (dyes, explosives, etc.)	210
Unclassified haptens or haptens belonging to smaller groups*	800

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3. Method

3.1. Browsing Tools

HaptenDB has number of browsing tools. To help the users, home page displays three options of Hapten, Carrier, and Antibodies browsers for direct search.

3.1.1. Browsing Haptens

This option allows users to browse haptens in database. The users can click the hapten link provided on the home page, which will provide brief information about each hapten. Figure 1 shows the example output of this option that includes haptens, their synonyms, and modifications.

3.1.1.1. DETAILED DESCRIPTION OF HAPTEN

One gets brief description about hapten by clicking on browsing option, HaptenDB. As shown in Fig. 1, each hapten record has clickable button 'Detail,' where user can get detailed information about a hapten. An example of hapten 2,4-dichlorophenoxyacetic acid is shown in Fig. 2, while Table 3 shows the name and description of field.

3.1.2. Browsing Carrier

Similarly, on clicking the carrier option on home page, one would receive the output (Fig. 3) as a list of 25 different carriers with their name, nature, and sequence distributed over two pages.

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The screenshot shows the HaptenDB website interface. At the top, there is a logo and the text 'HaptenDB' and 'A comprehensive Web S'. Below this is a navigation menu with options like Home, HaptenDB, SRS at IMTECH, IMTECH HOME, Bioinformatics Centre, Raghava's Group, Search, Keyword Search, Structure, Sketch, Browse, Hapten, Carrier, Antibodies, Submit, Submit a Hapten, Submit an Antibody, About Us, Team Members, Contact Person, Help, Related Links, Information, and Help. The main content area is titled 'Browsing Haptens Page 1 of 44' and contains a list of six records, each with a 'Detail' button. The records are as follows:

Record No.	Hapten Name	Synonyms
1	2,4-Dichlorophenoxyacetic acid	2,4-D
2	Atrazine	2-Chloro-4-(ethylamino)-6-(isopropylamino)-s-triazine Atrazine(Pr/C/ET) R1 = (CH3)2-CH-NH- R2 = -Cl R3 = -NH-CH2-CH3
3	Nicotine	3-(1-Methyl-2-pyrrolidyl)pyridine, Black Leaf
4	Morphine	orphi, Morphine Sulfate
5	2,4-DINITROCHLOROBENZENE	1-Chloro-2,4-dinitrobenzene; DNCB; Dinitrochlorobenzene
6	(Structurally related s-triazines)	[Pr/C/C6 R1 = (CH3)2-CH-NH-

Fig. 1. Browsing of hapten molecules, an example output.

3.1.2.1. DETAILED DESCRIPTION OF CARRIER MOLECULE

Each carrier record has clickable button 'Detail,' which provides detailed description of a carrier molecule. An example record of avidin is shown in Fig. 4. The carrier is usually a high molecular weight protein attached with the hapten to provide it immunogenicity. The brief description fields are given in Table 4.

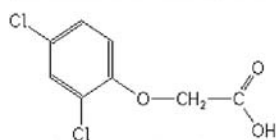
3.1.3. Browsing Antibodies

The clicking of antibody browser on the home page will show output as a list of 238 records of different antibodies with their name and type (Fig. 5) distributed over ten pages, and clicking the detail of any record will show output as a list of the entries for a particular antibody raised against same, related, or different haptens, along with the type and cross-reactivity of the antibody (inlay in Fig. 5). Finally, clicking the detail of particular antibody against the particular hapten will show the output (Fig. 6) as a table describing the properties of the antibody.

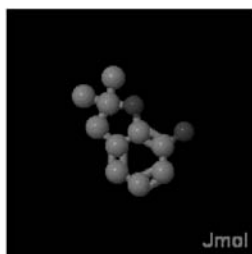
01 **Record No. 1**

02 Download as A Text File

03 Hapten Name	2,4-Dichlorophenoxyacetic acid
04 Synonyms	2,4-D
05 Molecular Formulae	C ₈ H ₆ Cl ₂ O ₃
06 Physical Properties	Colour: WHITE TO YELLOW CRYSTALLINE POWDER Odour: ODORLESS WHEN PURE Boiling Point: 160 DEG C AT 0.4 MM HG Melting Point: 138 DEG C Density: 1.416 @ 25 deg C
07 Nature	Pesticide (Herbicide)
08 Molecular Weight	221.04
09 Toxicity	Toxic
10 Area of Uses	AS A HERBICIDE FOR CONTROL OF BROADLEAF PLANTS & AS A PLANT-GROWTH REGULATOR. HERBICIDE USED ON GRASSES, WHEAT, BARLEY, OATS, SORGHUM, CORN, SUGARCANE, & NONCROP AREAS PASTURE AND RANGE LAND; It is used on tomatoes to cause all fruits to ripen at the same time for machine harvesting. /2,4-D free acid serves as the basic material from which the soluble esters & salts are produced. Used in forest management: Brush control; Conifer release; Tree injection. To increase latex output of old rubber trees. Fruit drop control



Download Structure in 2D/3D MOL Format



27 Fig. 2. The details of particular hapten (2,4-dichlorophenoxyacetic acid in this case).

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29 The table showing antibody details is a comprehensive table to make one
30 understand the major aspects covered in a particular paper completely. It starts
31 with the name of the hapten, its synonym, modifications, if any, followed by
32 the details of antibody generation, and its characterization. Following is the
33 description of fields (see Fig. 6).

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1. Hapten Name: Common name of haptenic compound.
 2. Synonyms: Its chemical name or other commonly used names.
 3. Modification: Modification in an existing well-known compound by introducing some groups or replacing one group with other.
 4. Conjugation Method: The method used for the conjugation of hapten with the carrier molecules.

01 **Table 3**
02 **Detail description of each field**

03 Field name	Description
05 Hapten name	It displays the common name of haptenic compound.
06 Synonyms	This shows the chemical name or other commonly used names.
07 Modification	This specifies the modifications, if any, in an existing well-known compound by introducing some groups or replacing one group by the other.
08 Molecular formulae	Molecular formula of the hapten
09 Physical properties	This describes the physical properties in terms of its color, odor, boiling point, melting point, and density.
10 Nature	This gives nature or category of the haptenic compounds, e.g., pesticide, drug, peptide, hormone, and vitamins.
11 Molecular weight	Molecular weight of the compound.
12 Biological activity	It describes the effect of the compound in terms of toxicity on biological system.
13 Area of uses	This field contains information about the different uses of the hapten and their actions.
14 Structure	This field displays 2D (Fig. 3) and 3D (Fig. 4) structure of hapten. Jmol has been integrated into the database for the display and manipulation of 3D structures. Moreover, the structures could be downloaded in the form of Mol files.

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- 28 5. Conjugation Method Details: They are well-defined protocols that are usually
- 29 used with some modifications and are cited in literature, for example, active ester
- 30 method and mixed anhydride method. Either the details or the reference of the
- 31 paper is provided.
- 32 6. Spacer/Linkage Nature: The spacer arm, if any, attached to hapten before conju-
- 33 gation to carrier molecules. As regard to linkage nature, the nature of bond between
- 34 the hapten and the carrier molecule, for example, amide linkage.
- 35 7. Hapten Carrier Ratio: It shows number of haptens attached per molecule of carrier.
- 36 8. Antibody Name: Name of the antibody that is raised against hapten.
- 37 9. Host organism: The host used to raise antibodies, that is, mouse, rabbit, goat, etc.
- 38 10. Type & Class: It is the type of antibody that is raised in the host organism,
- 39 for example, monoclonal, polyclonal, or only antiserum. In case of monoclonal antibodies, the details of isotypes are also described.

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HaptenDB
:: A comprehensive Web Server for Haptens, Associated Carrier Proteins and Hapten Antibodies :: HaptenDB

Home
:: HaptenDB
:: SRS at IMTECH
:: IMTECH HOME
:: Bioinformatics Centre
:: Raghava's Group
Search
:: Keyword Search
:: Structure
:: Sketch
Browse
:: Hapten
:: Carrier
:: Antibodies
Submit
:: Submit a Hapten
:: Submit a Antibody
About Us
:: Team Members
:: Contact Person
Help
:: Related Links
:: Information
:: Help

HELP
Next

Browsing Carriers Page 1 of 2

Record No. 1 Detail

Carrier Name	Avidin
Carrier Nature	Protein (glycoprotein)
Carrier Sequence	http://www.ncbi.nlm.nih.gov/entrez/viewer.fgi?db=protein&val=53717952

Record No. 2 Detail

Carrier Name	DTG
Carrier Nature	Protein
Carrier Sequence	http://www.ncbi.nlm.nih.gov/entrez/viewer.fgi?db=protein&val=27865935

Record No. 3 Detail

Carrier Name	Bovine G globulin
Carrier Nature	Protein

Record No. 4 Detail

Carrier Name	Bovine Immunoglobulin G (IgG)
Carrier Nature	Protein

Record No. 5 Detail

Carrier Name	Bovine Serum Albumin (BSA)
Carrier Nature	Protein
Carrier Sequence	http://www.ncbi.nlm.nih.gov/entrez/viewer.fgi?db=protein&val=3336842

Record No. 6 Detail

Carrier Name	Bovine-Thyroglobulin
Carrier Nature	Protein

Fig. 3. Browsing of carrier molecules, an example output.

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Record No. 1

Download as A Text File

Carrier Name	Avidin
Carrier Nature	Protein (glycoprotein)
Carrier Sequence	http://www.ncbi.nlm.nih.gov/entrez/viewer.fgi?db=protein&val=53717952
Physical Properties	synthesized in the hen oviduct, is a glycoprotein of MW 68,000 daltons which occupies about 0.05% (w/w) of the total protein content of the hen egg white. The isoelectric point of native Avidin is 10.5. Avidin, native or modified is very stable against heat, pH changes and chaotropic reagents (5). The Avidin solution is stable for weeks or a month at 4°C.

Fig. 4. The details of particular carrier molecule (avidin in this case).

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11. Cross-reactivity: Cross-reactivity of the raised antibodies with other similar or related compounds has been mentioned as IC_{50} value, where IC_{50} is referred to the amount required for 50% inhibition of the antibody in the given set of conditions.
 12. Sensitivity: This is also referred as limit of detection of the hapten with the raised antibody.
 13. Assay System: The method used for characterizing the antibodies, for example, competitive ELISA, noncompetitive ELISA, and RIA.
 14. Application: Likely application and future prospects of the ELISA method developed, antibody raised, etc.

Table 4
Description of fields of carrier record

Field name	Description
Carrier name	The name of the carrier
Nature	The nature of the protein such as, glycoprotein, and lipopeptide.
Sequence	The sequence of the protein. For this, the NCBI GENPEPT link is provided from where one can retrieve the information about the sequence, source, and origin of the carrier.
Physical properties	In terms of the molecular weight and any specific property for its advantage as carrier protein.

The screenshot displays the 'Browsing Antibodies' interface on 'Page 1 of 10'. It features a list of antibody records on the left and a detailed view of a selected antibody on the right. The 'Browsing Antibodies' section lists records 1 through 7, each with fields for Antibody Name and Antibody Type. Record 1 is selected, and its details are shown in the 'Searched Antibody' section, including fields for Antibody name, Hapten Name, Antibody Type, and Cross Reactivity.

Record No.	Antibody Name	Antibody Type
Record No. 1	I409, Anti 3-methylindole antibodies	Monoclonal antibody
Record No. 2	DF12, Anti 3-methylindole antibodies	Monoclonal antibody
Record No. 3	441G, Anti 3-methylindole antibodies	Monoclonal antibody
Record No. 4	DF2, Anti 3-methylindole antibodies	Monoclonal antibody
Record No. 5	BH1, Anti 3-methylindole antibodies	Monoclonal antibody
Record No. 6	Anti-Fumonisin B1 antibodies	Antiserum
Record No. 7	Anti-Bactracin antibodies	Antiserum

Record No.	Antibody name	Hapten Name	Antibody Type	Cross Reactivity
Record No. 1	I409, Anti 3-methylindole antibodies	3-methylindole	Monoclonal antibody	100%
Record No. 2	I409, Anti 3-methylindole antibodies	3-methylindole Derivatives	Monoclonal antibody	
Record No. 3	I409, Anti 3-methylindole antibodies	Indole	Monoclonal antibody	31.4%
Record No. 4	I409, Anti 3-methylindole antibodies	Indole Derivatives	Monoclonal antibody	49.1%
Record No. 5	I409, Anti 3-methylindole antibodies	Indole Derivatives	Monoclonal antibody	

Fig. 5. Browsing of antibodies in HaptenDB, a screen shot from HaptenDB after clicking on “Browsing Antibodies.”

- Reference: This field has the details of the journal, author, title, volume, page numbers., and year of publication of the paper in which this information is reported.
- Web link: This field contains the web link of the research paper that is cited in the reference field.
- Comments: This field contains other relevant information that is not contained in all the above-mentioned fields such as immunization protocol, some other important properties of antibody, hapten, or carrier.

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Record No. 1	
Download as A	Text File
Hapten Name	3-methylindole [Detail]
Antibody Name	14G8, Anti 3-methylindole antibodies [More Info]
Host Organism	BALB/c mice (4-9 month old)
Antibody Type	Monoclonal antibody
Cross-reactivity	100%
Assay System	Non-competitive time-resolved fluoroimmunoassays Competitive time-resolved fluoroimmunoassays
Reference	M Tuomola, R Harpio, H Mikola, P Knuutila, M Lindstrom, V M Mikkala, M T Matikainen, T Lovgren : Production and characteris Immunological Methods : 240, 111-124 : 2000
Web Links	http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T2Y-40GHRXB-C&_user=529620&_coverDate=06%2F23%2F2000&_alid=112964107&_rdoc=1&_fmt=summary&_orig=search&_cdi=4931&_sort=d&_st=4&_docanchor=&_acct=C00002
Comments	1) The antibody are produced against 3-Methylindole. 2) Cross Reactivity is calculated as a ratio of IC50 value of 3-Methylindole with IC50 value of cross reacting compound setting

15 Fig. 6. Table showing detailed information of an antibody, a screen shot.

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Search HaptenDB

Keywords to search

Keywords : within within

Conditions

e.g.

Hapten : Atrazine
Antibody : Anti-simazine
Author/Title : Hammock
Hapten Nature : Pesticide
Emperical formulae : C8H6Cl2O3

Select in which Compound Category you want to Search

Search in this group of Compounds
 Pesticides, Herbicides, Insecticides etc.
 Drugs, Vitamins
 Steroids, Hormones
 Toxins

Experiments performed in

No. of results per page

Click to perform search
Click to reset the form data

Fig. 7. Keyword search page of HaptenDB.

3.2. Searching Options

As browsing tools allow one to see the records as they were entered in the database. It is difficult to search a specific hapten or antibody or carrier using the browsing tool. HaptenDB also has searching facility, in order to assist the user in getting a specified hapten. The searching facility includes (i) keyword search and (ii) structure similarity search.

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3.2.1. Keyword Search

Using this search engine, one can specify a search by giving keywords. The keyword, that is, input (Fig. 7), could be the name of the (i) hapten, (ii) antibody, (iii) author, (iv) title of the paper, (v) nature of the hapten, and (vi) empirical formula of the hapten. The users can also specify the category of the hapten: (i) all compounds; (ii) pesticides, herbicides, and insecticides; (iii) drug and vitamins; (iv) steroids and hormones; and (v) toxins and the host organism in which antibody is raised as (i) all hosts, (ii) mouse, (iii) sheep, and (iv) rabbit. Moreover, results per page can also be specified as desired: (i) 10, (ii) 25, (iii) 50, or (iv) 100 results per page. Figure 8 shows the keyword search, that is, output for the atrazine and the options to filter the search.

Your Query Fetched 296 Records

Click to Download the search result as a text file

Download as A Text File

Click to move to next search page

HELP

Page 1 of 12

Next

Click to view the details of this record

Click to view the details of hapten

Click to view the details of this carrier molecule

Record No. 1 <i>Detail</i>	
Hapten Name	Atrazine [Detail]
Carrier Name	Bovine Serum Albumin (BSA) [Detail]
Antibody Name	Anti-Atrazine antibodies [More Info]

Click to view the detailed summary of all records related to this antibody

Record No. 2 <i>Detail</i>	
Hapten Name	Atrazine [Detail]
Antibody Name	Anti hydroxyatrazine antibodies (HYB-283-2) [More Info]

Record No. 3 <i>Detail</i>	
Hapten Name	Atrazine [Detail]
Carrier Name	Keyhole Limpet Hemocyanin (KLH) [Detail]
Antibody Name	Anti Atrazine Antibodies (In Rabbit/Sheep) [More Info]

Record No. 4 *Detail*

Fig. 8. An example output page of keyword search.

3.2.2. Structure Search

One of the powerful tools integrated in HaptenDB is structure similarity tool, which allows user to search similar hapten structures. The similarity search option can be divided into two categories: (i) upload and search structure and (ii) sketch and search the structure.

The screenshot displays the 'Search HaptenDB using Hapten Structure' interface. It includes an 'Upload Structure' field with a 'Browse...' button, a 'Similarity Type' dropdown menu set to 'Substructure search', and 'Reset' and 'Submit' buttons. Below the form is a note: 'Note : Users must submit the structure in chemical structure formats such as mol, pdb etc.[More] and not as images of structures. *Similarity search is done using Java based jsearch command line utility of JChem for more information in this regard visit www.jchem.com.' The search results section is titled 'Your Query Fetched 318 Records' and includes a 'Download as A Text File' link, a 'Page 1 of 13' indicator, and a 'Next' button. The results are presented as a list of records, each with a 'Detail' link and a table of Hapten Name and Antibody Name.

Record No. 1 <i>Detail</i>	
Hapten Name	2,4-Dichlorophenoxyacetic acid [Detail]
Antibody Name	Anti-2,4,5-Trichlorophenoxyacetic acid antibodies [More Info]

Record No. 2 <i>Detail</i>	
Hapten Name	2,4-Dichlorophenoxyacetic acid [Detail]
Antibody Name	Anti Isoproturon Antibodies [More Info]

Record No. 3 <i>Detail</i>	
Hapten Name	2,4-Dichlorophenoxyacetic acid [Detail]
Antibody Name	Anti-(Delor 103) antibodies [More Info]

Record No. 4 <i>Detail</i>	
Hapten Name	2,4-Dichlorophenoxyacetic acid [Detail]
Carrier Name	Bovine Serum Albumin (BSA) [Detail]
Antibody Name	Anti (2,4-Dichlorophenoxyacetic acid) Antibodies [More Info]

Record No. 5 <i>Detail</i>	
Hapten Name	2,4-Dichlorophenoxyacetic acid [Detail]
Carrier Name	Thyroglobulin (Tg) [Detail]
Antibody Name	Anti-2,4-Dichlorophenoxyacetic acid(MAbs `s B5/C3, E2/B5, E2/G2, F6/C10, and F6/E5) [More Info]

Record No. 6 <i>Detail</i>	
Hapten Name	2,4-Dichlorophenoxyacetic acid [Detail]
Carrier Name	Bovine Serum Albumin (BSA) [Detail]
Antibody Name	Anti (2,4-Dichlorophenoxyacetic acid) Antibodies [More Info]

Fig. 9. Searching of similar structures, an example input and output screens of HaptenDB.

01 UPLOAD AND SEARCH STRUCTURE

02 This option allows one to search their structure against hapten structure.
03 In order to use this option, one needs to have structure in standard format
04 readable by BABEL software. One needs to upload the structure file to be
05 searched and to select appropriate options that include type of similarity search
06 (e.g., substructure, superstructure, perfect, or exact search). The output (Fig. 9)
07 will provide the list of haptens and the corresponding antibodies satisfying the
08 criteria of the search (substructure search in this case), and again clicking the
09 detail will lead to the detail of hapten or antibody.
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11 SKETCH SEARCH

12 The database integrates JME molecular editor, using which one can sketch
13 the structure of the query molecule instead of the uploading of the file. This
14 option is very useful for creating and searching similar structure. Figure 10
15 shows the input for the chlorobenzene sketch search and submit for the
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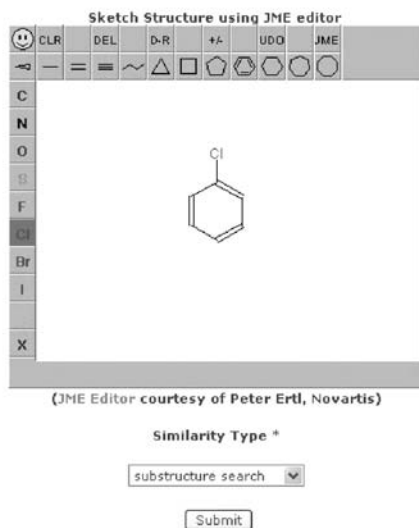
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Search HaptenDB using Hapten Structure



Note : * Similarity search is done using Java based jsearch command line utility of JChem for more information in this regard visit www.jchem.com.

Fig. 10. A screen shot of sketching structure using JME editor.

01 similarity search as above; however, output would be the same (Fig. 9) as in
02 case of structure search.

03 04 **Acknowledgments**

05 We acknowledge the financial support from the Council of Scientific
06 and Industrial Research (CSIR) and Department of Biotechnology (DBT),
07 Government of India.

AQ5

08 09 **Notes**

- 10 1. The users are required to fill a request form available at
11 <http://www.imtech.res.in/errors/noauth.html> for using web servers developed by
12 Raghava's group (<http://www.imtech.res.in/raghava/>).
- 13 2. It is difficult for developers to maintain any database without the help of the
14 scientific community. Users are requested to submit their new haptens.
- 15 3. Each page of the database is self-explanatory; still to help the user "Help" option
16 is provided on the home page as well as individual pages.
- 17 4. Database have Related Links, which gives the web links of the sites either used for
18 the construction of the database or could be useful for the browser in one or the
19 other way.
- 20 5. Information option gives the information about the architecture of the database,
21 category-wise analysis of database, data management of HaptenDB, system
22 requirement to access, data submission and updates, and disclaimer and limitation
23 of liability.

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UNCORRECTED PROOF

01 **QUERIES TO BE ANSWERED (SEE MARGINAL MARKS)**

02
03 **IMPORTANT NOTE: Please mark your corrections and answers to these**
04 **queries directly onto the proof at the relevant place. Do NOT mark your**
05 **corrections on this query sheet.**

06
07
08 Chapter-08

09

10 Query No.	Page No.	Line No.	Query
11 AQ1	123	31	In the sentence “These carrier molecules provide T lymphocyte help required for the induction of humoral (antibody) response”, please clarify whether the text “T lymphocyte help” is OK.
16 AQ2	124	23	The sentence “HaptenDB, first of its kind, aims at providing the information to the user about the haptens with respect to its chemical, physical, and structural properties” has been rephrased. Please check if it is OK.
22 AQ3	126	Table 2	In Table 2, please provide the significance of the footnote-linking symbol “*”.
25 AQ4	133	04	Please clarify whether the sentences ‘As browsing tools allows one to see the records as they were entered in the database. It is difficult to search a specific hapten or antibody or carrier using the browsing tool’ could be changed to ‘As browsing tools allows one to see the records as they were entered in the database, it is difficult to search a specific hapten or antibody or carrier using the browsing tool’.
37 AQ5	136	09	Please provide the citations for all the Notes.

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