PUBLISHED DATABASE MINING FOR MMP-2 INHIBITORS  
(NATURAL AND SYNTHETIC).

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ABSTRACT

With reference to importance of the MMP-2 in study of all types of the cancer, it is must to summarize all the data at a single place. This place may be as hard copy on paper. But due to large data it is impossible to keep data as hard copy. So we have another very convenient place that is world wide web (WWW) on internet. On internet we can save any amount of data and also we can easily get data of our need. So WWW/internet is soul of all type of information we need or we have online. In next step in data collection at one place, we need data mining for required data. The data should be collected from the authentic place like reputed databases, journals etc. Here we explored all databases having information regarding MMP-2 inhibitors (natural and synthetic).

KEYWORDS: Database, data-mining, journal, MMP-2, Natural Inhibitors, Synthetic Inhibitors.

INTRODUCTION

Matrix metallo-proteinases (MMPs) are plays most important role in regulated degradation of extracellular matrix (ECM) with development, morphogenesis, tissue repair and remodelling. On other hand dis-regulation of MMPs causes different kind of diseases including deadly cancer, arthritis, nephritis, encephalomyelitis, chronic ulcers, fibrosis, etc. The upregulation of MMPs are inhibited by endogenous inhibitors, tissue inhibitors of metalloproteinases.
TIMPs). Thus, the balance between MMPs and TIMPs are critical for the eventual ECM remodelling in the tissue.\textsuperscript{[2]} In continuation towards the natural MMP inhibitors, more than 20,000 new compounds have been isolated from nature considered as potential candidates for pharmaceutical application. Saccharoids, flavonoids and polyphones, fatty acids are the most important groups of MMPIs derived from marine natural products.\textsuperscript{[3]} The matrix metalloproteinases (MMPs) in humans are a family of 28 members that have classically been associated with remodeling of the extracellular matrix (ECM). Because of their involvement in processing of the ECM, MMPs were implicated in cancer invasion and metastasis.\textsuperscript{[3,4]} Consistent with this hypothesis, multiple data from model systems suggested that specific MMPs were causally involved in metastasis.\textsuperscript{[3,4]}

The involvement of MMPs in cancer dissemination led to the development of MMP inhibitors (MMPIs) for the treatment of malignancy.\textsuperscript{[5–7]} Although these inhibitors reduced or blocked the formation of metastasis in animal models, results from clinical trials were disappointing due to poor efficacy and toxic side-effects.\textsuperscript{[5–7]} Indeed, in some studies, there were suggestions that the MMPIs may have promoted cancer progression.\textsuperscript{[7]} These disappointing findings lead to a reconsideration of the role of MMPs in cancer and prompted detailed studies on specific MMPs in preclinical cancer models. Somewhat surprisingly, this research suggested that certain MMPs, rather than promoting cancer, were inhibitory against cancer, at least in some situations.\textsuperscript{[8–10]} Thus, the current thinking, on the basis of animal models, is that while some MMPs promote cancer formation/progression, others inhibit this process.\textsuperscript{[8–10]} If MMPIs are to be used in the treatment of cancer, it is important to know which members promote and which protect against malignancy. In an attempt to address this question, we used published databases to carry out a detailed investigation of MMP-2 Inhibitors.

**MATERIALS AND METHODS**

This insilico study was carried out with use of all required facilities at Department of Pharmacology & Therapeutics, King George’s Medical University, Lucknow.

**Computer and Internet Connection**

The study was completely in-silico off-course with the use of computer and here there is no need to introduce the computer because now it becomes necessity for today’s life. Whenever and wherever we talk about the computer we can’t ignore the internet i.e. world wide web (WWW), because without internet there disconnection from the world. Hence we used the
computer for the structure analysis by different programs and internet for gathering the information to complete the study.

**Databases**

All the information regarding MMP-2 was explored from the different freely available biological databases. The information may be in the form of information/structure/domain of the MMP-2. These different freely available online databases were PDB, MMPdatabase, NCBI, EXPASY, UNIPROT, INFORMATICS, Wikipedia etc.

**Journals**

All search made through WWW was with the reputed journal available online. These reputed journals should have registered with any academic society or organization with some registration id and also evaluated by impact factor by some evaluation organizations.

**RESULTS**

We tried my best for WWW search for the MMP-2 inhibitors (natural and synthetic) resulting 144 inhibitors (both natural & synthetic) (Tab. 1).

**Table 1: List of Natural and synthetic MMP-2 Inhibitors**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Inhibitor’s name</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(+)-Aeroplysinin-1</td>
<td>Natural</td>
</tr>
<tr>
<td>2.</td>
<td>1-(3′,5′-dihydroxyphenoxy)-7-(2″,4″,6″-trihydroxy-phenoxy)-2,4,9-</td>
<td>Natural</td>
</tr>
<tr>
<td></td>
<td>trihydroxydibenzo-1,4,-dioxin</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>2dieckol</td>
<td>Natural</td>
</tr>
<tr>
<td>4.</td>
<td>3-(3, 4-dihydroxy-phenyl)-acrylic acid phenethyl ester (caffeic acid phenethyl ester,CAPE)</td>
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</tr>
<tr>
<td>5.</td>
<td>3-azidowithaferin A (3-azidoWA)</td>
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</tr>
<tr>
<td>6.</td>
<td>474</td>
<td>Synthetic</td>
</tr>
<tr>
<td>7.</td>
<td>6,6′-bieckol</td>
<td>Natural</td>
</tr>
<tr>
<td>8.</td>
<td>ABT-518</td>
<td>Synthetic</td>
</tr>
<tr>
<td>9.</td>
<td>acetohydroxamic acid</td>
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</tr>
<tr>
<td>10.</td>
<td>Acetylsalicylic acid</td>
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</tr>
<tr>
<td>11.</td>
<td>Actinonin</td>
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</tr>
<tr>
<td>12.</td>
<td>Ad-MMP2-si</td>
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</tr>
<tr>
<td>13.</td>
<td>ageladine 9</td>
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<td>14.</td>
<td>Ägeladine A</td>
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<td>15.</td>
<td>Alendronate</td>
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<td>16.</td>
<td>Aloin</td>
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<td>17.</td>
<td>Amlodipine (Ca2+ channel blocker)</td>
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<td>Anthothele</td>
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<tr>
<td>19.</td>
<td>Anthocyanins</td>
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<tr>
<td>20.</td>
<td>Apigenin</td>
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</tr>
<tr>
<td></td>
<td>Name</td>
<td>Type</td>
</tr>
<tr>
<td>---</td>
<td>-----------------------------------</td>
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<td>Artemisinin</td>
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<tr>
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<td>Bisphosphonates</td>
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<td>C27H33N3O5S</td>
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<td>Caffeic acid</td>
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<td>37.</td>
<td>Callysponginol Sulfate A</td>
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<td>38.</td>
<td>Captopril (ACEi)</td>
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<td>carboxylated Chitooligosaccharides (CCOS)</td>
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<td>48.</td>
<td>Clitoria ternatea</td>
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<td>79.</td>
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<td>80.</td>
<td>Isorhamnetin 3-O-b-D-glucosides.</td>
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<td>81.</td>
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<td>82.</td>
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<td>85.</td>
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<td>86.</td>
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<td>Metastat/CMT-3</td>
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<td>102.</td>
<td>OPB-3206</td>
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<td>116.</td>
<td>Ro 31-9790</td>
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DISCUSSION

Several studies have previously investigated the potential prognostic impact of individual MMPs in different cancer.\textsuperscript{[11-18]} Most of these studies were retrospective and contained small numbers of poorly defined patient populations. In the different studies, a variety of cut-off points were used to differentiate patients with poor and good outcome. Few, if any of the findings, have been validated in external patient populations.\textsuperscript{[19-36]} Our analysis of a published database for the MMP-2 inhibitors (Natural & Synthetic) against the human prostate cancer. Most of the MMPs associated with adverse outcome in this study had previously been investigated in preliminary studies for potential prognostic value in breast cancer.

CONCLUSION

Although we have a good number of inhibitors present against the MMP-2, but still we do not have any specific inhibitor neither natural nor synthetic to give satisfactory results by
inhibiting the MMP-2 against the prostate cancer. So we should have more researches to give some specific MMP-2 inhibitor.

REFERENCES

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