Analysis of Patents Pertaining to Superdisintegrants used in Tablet Manufacturing

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The objective of the present investigation is application of patent analysis tool in planning research on superdisintegrants in pharmaceutical tablets. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The major function of the disintegrants is to appose efficiency of the tablet binder and physical forces that act under compression to form the tablet. Superdisintegrants generally are used at low level in solid dosage forms, typically 1-10% by weight relative to the total weight of the dosage unit. They are important in formulation of novel tablet dosage forms like mouth disintegrating tablets. Not all research gets published in papers and a lot of information is made available to the public through patents. A detailed analysis of the granted patents as well as patent applications can provide information that may otherwise be found critical however, missing. By analysing patents on superdisintegrants, research gaps can be identified and the research work to be taken up can be focussed. A complete analysis of the patents granted on superdisintegrants was done using various criteria such as patenting trends over the years, country wise distribution and different classes of superdisintegrants.

Keywords: Patent analysis, superdisintegrants, activity index

Scientists in research institutions and academics often come across the scientific literature in peer reviewed journals. However, this literature at times tends to provide insufficient objective information on the technological strategies being adopted by the commercial companies in their research laboratories. This is because of the fact that technologies during their development phase are often protected by proprietary secrecy and are least visible.

A systematic analysis of patents may provide some of the missing information. It provides a unique planning resource for managing R&D projects. One potential use of patent trend data is in evaluating the technological importance of a particular concept, process or product and their improvements. Consequently, in R&D programmes, the research approach should be seriously compared with others in terms of uniqueness, cost effectiveness and market acceptance. Systematic examination of other patents in the same research area can help in making this comparison.

Patent analysis can lead to a better awareness and improved effectiveness of creative ideas and R&D resource allocation. Patent information is priceless. Patent compromise vast information resource being filed across the world in every area of technology. Patent information enhances business intelligence of an individual by insuring that time; efforts and resources are not wasted in duplicating already available research. This information also helps in keeping a close watch on competitors. It gives an indication of new developments and provides an insight into the R&D trends worldwide.

Patents in superdisintegrants were analysed to gain an understanding of the technical approaches taken by different research groups throughout the world doing research in the same area. Patent information on the ‘use of superdisintegrants’ is a tool for collection of data on the trends in the latest technologies and R&D trends worldwide in the field of use of superdisintegrants. This information helps to analyse the collected data in a global perspective.†

Technological Significance of Superdisintegrants

Although compressed tablets have been manufactured for more than 100 years and today are a single most widely used dosage form for the administration of drugs, systematic study of tablet disintegration and dissolution is about 25 years old.2-6 Disintegrants are substances or mixture of substances added to the drug formulation that facilitate the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants.5 Tablet disintegration has received significant attention as an essential step in obtaining rapid drug release. The emphasis on

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availability of a drug highlights importance of relatively rapid disintegration of a tablet as a criterion for ensuring uninhibited drug dissolution behaviour. Several factors affect the disintegration behavior of tablets.\textsuperscript{7,8,9}

The major function of disintegrants is to appose efficiency of the tablet binder and physical forces that act under compression to form the tablet. Stronger the binder, more effective must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared.\textsuperscript{10}

In the past, starch was one of the most widely used, inexpensive, and effective tablet disintegrant. However, a high concentration of starch is needed to bring about effective disintegration. The research carried out by several scientists has helped develop certain compounds as disintegrating agents with efficient disintegrating properties at low concentrations.\textsuperscript{8,11-13}

Superdisintegrants generally are used at low level in solid dosage form, typically 1-10\% by weight relative to the total weight of the dosage unit. Selecting appropriate formulation excipients and manufacturing technology can obtain the design feature of fast disintegrating tablet.\textsuperscript{14,15} Examples of superdisintegrants are Crosscarmelose, Crospovidone and sodium starch glycolate which are a crosslinked cellulose, crosslinked polymer and crosslinked starch respectively. Apart from these three popular superdisintegrants there are some other substances such as, ion exchange resins, gums and soy polysachharides which are also available.\textsuperscript{16} The superdisintegrant may be used alone or in combination with other superdisintegrants. Commercially available superdisintegrants are listed in Table 1.\textsuperscript{17}

The superdisintegrant is present in the tablet in an amount of upto 10\% by weight. The superdisintegrant may be a single superdisintegrant or a combination of superdisintegrants and is normally used in combination with one or more common disintegrants.

There is no particular upper limit regarding the amount of superdisintegrant as long as the mechanical properties of the tablet are compatible with its intended use. However, normally amount of superdisintegrant should not exceed 25\% by weight. From the cost point of view, amount of superdisintegrant should not preferably exceed 15-20\% by weight, as normally no particular benefits will be achieved beyond this range.The superdisintegrant may be present as an extra granular and/or as an intragranular component.\textsuperscript{18,19}

### Data and Methodology

Data for analysis was obtained from the patent database maintained by National Informatics Centre (NIC), New Delhi, as well as USPTO. This database consists of patent filed and granted in sixty-five countries in wide variety of fields. Patent search was made in both the databases for the years 1985 to 2006 using the keyword superdisintegrants.\textsuperscript{20-25} A total of 45 patents were obtained from NIC database and 35 from the USPTO database of which 28 patents were found common in both the databases.

### Growth of Patents over the Years

The output of patents during 1983 to 2006 was divided into 6 blocks (Table 2). The number of patents on the use of superdisintegrants increased in every block. Further, it was seen that Europe has major number of patents related to the use of superdisintegrants. Until today, 52 patents have been filed, out of which 20 are filed by Europe.

No. of patents filed with country wise-distribution is: European Union (20), United States (9), World patents (6), Australia (4), China (5), Canada (2) and other countries (6). These figures indicate that maximum patents on superdisintegrants were filed in

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of patents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983-1988</td>
<td>1</td>
</tr>
<tr>
<td>1989-1993</td>
<td>4</td>
</tr>
<tr>
<td>1994-1997</td>
<td>8</td>
</tr>
<tr>
<td>1998-2000</td>
<td>10</td>
</tr>
<tr>
<td>2001-2004</td>
<td>22</td>
</tr>
<tr>
<td>2005-2006</td>
<td>7</td>
</tr>
</tbody>
</table>

### Table 1 — Commercially available superdisintegrants

<table>
<thead>
<tr>
<th>Type of polymers</th>
<th>Commercially available brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium starch glycolate</td>
<td>Primogel, Explotab, Tablo, Vivastar</td>
</tr>
<tr>
<td>Cross-linked sodium carboxy methylcellulose</td>
<td>Ac-di-sol, Nymcel, Primellose, vivasol, solutab</td>
</tr>
<tr>
<td>Soy polysaccharide</td>
<td>Emcosoy</td>
</tr>
<tr>
<td>Crosslinked polyvinyl-pyrrolidone</td>
<td>Polyclasdone, Kollidon CL</td>
</tr>
<tr>
<td>Gellan gum</td>
<td>Kilcogel</td>
</tr>
<tr>
<td>Xanthan gum</td>
<td>Grindsted, Xanthan sm</td>
</tr>
<tr>
<td>Ion exchange resins</td>
<td>Indion 414, Tulsion 339, Amberlite IRP 88</td>
</tr>
</tbody>
</table>

### Table 2—No. of patents filed for superdisintegrants during 1983-2006
the European Union, followed by United States, world patents, Australia, China, and minimum in Canada.

Table 3 gives the data for different superdisintegrants used and number of patents. It is a combined data obtained from NIC and USPTO databases. From the table it can be seen that Amylose is the most widely patented superdisintegrant. Very little number of patents are found on formulations containing conventional superdisintegrants like Croscarmallose sodium, Crosspovidone, sodium starch glycolate and few ion exchange resins. This indicates that there is still a scope for exploring these superdisintegrants in pharmaceutical tablet formulations and patenting this research.

Activity Index

Activity index (AI) characterizes relative research effort of a country to a given subject field. AI=100 indicates that the country’s research effort in the given field corresponds precisely to the world average. AI>100 indicates higher activity than world average. AI< 100 indicates activity lower than the average effort in the specified field. However, in the present case it has been modified and has been used to calculate AI of Europe vs rest of the world.

\[
AI_{(of\;Europe)} = \left( \frac{\text{Europe output in a particular year/total Europe output}}{\text{world output in particular year/total world output}} \right) \times 100
\]

AI for European Union as compared to rest of the a world (AI=100) is given in Table 4.

European patents during the period 1983-2006 constitute about 38% of total patents filed over superdisintegrant.


The decrease in AI in Europe over the years 1997 to 2006 may be attributed to unavailability of the newer superdisintegrants for pharmaceutical tablets. But after the advent of the new era of superdisintegrants in the market, there is no significant rise in the AI which indicates that the pharmaceutical formulations using these newer superdisintegrants have not been studied and patented extensively. The number of Indian patents filed were found to be insignificant and indigenous excipients manufacturing companies producing disintegrants should focus their research in this area. There were no patents filed worldwide on ion exchange resin disintegrants which are widely being marketed for this purpose and this research area remains unexplored.

Conclusion

The study indicates that number of patents filed on superdisintegrants has increased significantly over the years 2001-2004. Maximum number of patents were filed in the year 2003 and in Europe. Maximum number of patents were filed on cross-linked N-vinyl 2-pyrrolidone (CLPVP) and sodium starch glycolate combination.

References

22 Xudong Xu, Oral disintegrants of isosorbide mononitrate and their preparation, Chinese Pat No. CN1582917, 23 February 2005.