In the past, HPLC and Dissolution were regarded as two separate analytical entities without any real possibility for hardware integration. This reluctance to integrate the two techniques was basically down to the time requirement needed for the manual manipulation of samples with (possible) manual dilution followed by sample injection into HPLC systems. With each chromatogram taking probably in the order of 10 minutes to elute, the thought of manually injecting a succession of 10 sets of six samples (plus blanks and standards) was plainly unattractive. This basically represented a 12 hour analysis period. UV measurement “online” (closed loop) was always going to be the first method of choice for unattended operation.

The advent of suitable fraction collectors made the first sample collection task a little easier, so that fraction collection was now able to at least remove samples from the dissolution vessels at specified intervals without user intervention. The ability to replenish removed medium was also a plus point in employing sample collection via a fraction collector. The need to conform to the 1% medium loss rule over the duration of the dissolution test was therefore satisfied.

However, the physical configuration of the fraction collectors was also an issue. Some collectors are round and therefore samples have to be moved to a suitable storage rack or to a secondary set of tubes following dilution. Manual dilution was prone to systematic errors and so, once again, the situation was on "hold".

The obvious benefits of multi-component analysis and lower limits of detection as offered by HPLC measurements alone were outmanoeuvred by the time investment required to complete what was essentially a semi-automated analysis.

Pharma Test WinDiss32-V3 offers the best hardware / software integration solution for total automated analysis. The need for more reliable automation and the advent of more sophisticated sample collection and handling is a situation that the Pharma Test WinDiss32-V3 software suite can handle with ease.
Online HPLC System for automated Tablet Dissolution Testing

The WinDiss32-V3 integrated solutions provide a unique analytical system for customers to configure analysis for online and offline Dissolution testing using Pharma Test Dissolution instruments, ASP 2000 Sample Processing Unit and an Agilent HPLC using Chemstation™ software or a Waters™ System using Empower CDS software.

And that is it. Let the system take care of the rest. The automatic tablet drop magazine makes sure that the tablets are dropped synchronously when required. The dissolution tester will start automatically and see that tool speed and bath temperature are maintained throughout the test. Samples can be transferred via a pump or syringe transfer module to the collection arm of the ASP 2000. The sets of collection tubes or HPLC vials will be filled in rotation. Sample tubing is emptied after every sample transfer, ready for the next sample set. An intelligent Z axis arm on the ASP 2000 now starts with sample transfer with or without dilution. If dilution is required then this is accomplished by transfer, dilution and mixing in a second set of vials. In the meantime, if a second set of samples is to be collected, then the Z axis arm will put the sample processing step on hold and then wait for the signal to start the pump and make a sample transfer from the dissolution vessels. Once finished, the sample processing will recommence. Injection into an HPLC pump is handled by the software.

**Full Communication**

ALL data is collected: bath and vessel temperatures, tool speed rates, measured UV absorptions, calculated % of API dissolved, mg of API dissolved and current COMBINED Dissolution / HPLC status are displayed live on screen at all times.

WinDiss32-V3 integrated solutions provide two way communication with Chemstation and Empower. Results are calculated in real time and are stored using the power of Oracle™ database and are available anywhere on the company’s network that has an WinDiss32-V3 integrated solutions client installed.

This Automated Tablet Dissolution Analytical System provides unprecedented performance over and above that of any other HPLC dissolution system.

**Full Flexibility**

- Online HPLC Systems can be configured using Baths from PharmaTest, Caleva, Distek, Erweka, Hanson, Sotax and Varian
- Automation of USP dissolution methods 1, 2, 3, 4 and 7; and not just 1 and 2 as with other systems
- Real time display of Dissolution data throughout the analysis, graphically and numerically
- Samples can be diluted and treated prior to injection or just after collection
- Uses existing HPLC methods
- Sample Sets or Sequence Tables are created automatically and managed by WinDiss32-V3 integrated solutions
- Reprocessing to allow for post analysis changes
- Re-measurement of specific Samples
- Automation of pH and Media change.
Realise the return on your investment with our data management system using the power of Oracle 10g database. Applications are configured under the security and compliance stipulated for 21 CFR part 11 and with features over and above that of our competitors. From setting user access to configuration for electronic signing, this seamless integration allows the system administrator to easily manage compliance issues; and with simplicity for users performing day to day analysis.

**One Software Solution...**

For the first time ever, WinDiss32-V3 is able to provide an online HPLC Tablet Dissolution system with Agilent Chemstation or Water Empower which satisfies Quality Control and Development requirements for automation (with pH measurement if required) throughout the analysis using Oracle database and with the possibility to Network data stations.

**WinDiss32-V3 integrated solutions provides the following...**

- The most comprehensive dissolution software available today
- Meeting the quality standards and Validation requirements of the Pharma Industry
- Choice of different dissolution Baths
- Choice for Agilent or Water HPLC
- Oracle database storage for data integrity, security and scalability
- Network database management for data centralisation and availability

**Online HPLC Dissolution Testing...**

The WinDiss32-V3 *integrated solutions* system can control nearly all dissolution Baths, Pumps and Filter Stations with Agilent or Waters HPLC.

This system configuration provides a two-way communication with Chemstation/Empower™ Software. The WinDiss32-V3 *integrated solutions* methodology is far in advance of any other HPLC dissolution system and allows for Multi-Component analysis with unlimited sampling Intervals, Sample Grouping with individual group statistics for product comparison, Dilution, Mixing and Sample conditioning prior to measurement.

The WinDiss32-V3 *integrated solutions* is currently the only dissolution system to allow the user to create and automate multiple pH and Media changes. Results, which comprise Area / Height values, %Dissolution, Temperature, Speed or pH etc., are displayed numerically and graphically in real time as the experiment proceeds.

During the analysis, results for each sample measured are stored in the Oracle Database thus protecting data already acquired in case of power failure.

**System configuration...**

A typical system configuration is shown below and consists of a Dissolution Bath, Pump, the ASP 2000 Analytical Processing Workstation and an Agilent HPLC Pump with Detector. The maximum or available functionality of each instrument is utilized. For example, temperatures for Baths with Vessel Temperature probes will show all temperatures for each Vessel while those with only one bath probe will only display a single temperature.
Intelligent Driver Interface…

The HPLC Driver with Chemstation or Empower provides an intelligent two way communication using a DDE interface with WinDiss2-V3 and Chemstation/Empower. Use three easy steps to set up your DDE:
First install a driver in the WinDiss2-V3 Driver Configuration Management.
A search can be performed on the Network or a name or TCP / IP addresses can be entered to locate the Workstation(s) where Chemstation/Empower is installed.
Once the workstation has been installed, a search for all HPLC Systems on the Workstation selected will occur. Select your HPLC system of choice
At the start of the analysis, the WinDiss2-V3 integrated solutions method will show all HPLC Systems installed on the workstation and will establish communications with the Chemstation/Empower controlled HPLC System selected.
A list of all methods on the HPLC System selected will then appear. Once a method is selected for the analysis, certain parameters from the method, i.e., the processing time is acquired from the HPLC method and used as part of the timing sequence in the analysis.

**Multiple Standards with Standard Bracketing and System Suitability...**

Multiple Standards can be configured as shown below. Standards can be configured and read at the beginning of the analysis or configured to be read through the analysis.

Any combination of these standards can be used for calculation or configured for System suitability.

Standards used here for calculation are a combination of a Standard read at the beginning of the analysis and those read through the analysis.

Users can configure these standards specific to their analytical requirements.
Acquisition of Dissolution Bath Parameters…

Temperature and Speed are acquired from the Dissolution Bath throughout the analysis. These can be acquired more frequently than the Sampling or Time Interval. Many other options for Dissolution / HPLC do not allow the transfer of dissolution test specific parameters such as tool speed, vessel temperature and bath temperature to be transferred into the HPLC software so there is no confirmation at any point that the dissolution bath was actually running.

All Baths configured will be controlled automatically. Details such as Temperature, Speed and in some cases pH are acquired during the analysis and can be displayed to the user in real time. An example is illustrated below.

![Sample Temperature Values](image)

System Control and Real Time Display of Results…

The ASP2000 Automated Workstation allows simultaneous operations for Sampling, Dilution, and Injection into the LC system. After each injection, the HPLC system perform the processing and the integrated values or results are acquired from Chemstation/Empower. The dissolution profile is updated and displayed numerically and graphically in real time on WinDiss32-V3 integrated solutions workstations.

There is no need for any manual intervention once this system has started.

Using a special Deferred Data Collection™ sequence, Samples Collected can be Diluted, Mixed and Injected while still maintaining accurate Collection times, thus delivering analysis in faster time periods.

The example illustrated below shows a 2 component mix of Aspirin and Paracetamol and the real time calculation from the HPLC peak area integration of the dissolved API along with the display of the dissolution profiles for both components.

Dissolution data Area values for two Components for a pharmaceutical product. The data is cached to the Oracle database as soon as it is collected.
Data, Area / Height values, Temperature, Speed and pH if configured, which are acquired during the analysis, are displayed in real time as shown above. From the Area / Height values, the %Dissolution is calculated and displayed in real time.

If the systems are networked, results on any workstation can be loaded remotely on any other WinDiss32-V3 integrated solutions workstation.

**Display of Compliance Table and Ranges Graphically...**

During the analysis or after the test has completed, the compliance table indicating whether the test has passed or failed can be displayed graphically or numerically. This is a very important tool for Quality Control and for Stability studies.

Below is an example of a Specification Compliance Table – Multiple Specifications can be configured for different pharmacopoeia requirement

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Lower</th>
<th>Upper</th>
<th>Sample 1</th>
<th>Sample 2</th>
<th>Sample 3</th>
<th>Sample 4</th>
<th>Sample 5</th>
<th>Sample 6</th>
<th>Pass/Fail</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.10:00</td>
<td>40.00</td>
<td>55.00</td>
<td>47.09</td>
<td>46.74</td>
<td>47.09</td>
<td>49.68</td>
<td>50.50</td>
<td>51.20</td>
<td>Pass</td>
</tr>
<tr>
<td>0.15:00</td>
<td>60.00</td>
<td>75.00</td>
<td>65.92</td>
<td>68.20</td>
<td>68.55</td>
<td>67.50</td>
<td>62.97</td>
<td>63.86</td>
<td>Pass</td>
</tr>
<tr>
<td>0.20:00</td>
<td>75.00</td>
<td>85.00</td>
<td>85.68</td>
<td>78.84</td>
<td>76.40</td>
<td>80.58</td>
<td>78.49</td>
<td>80.56</td>
<td>Pass</td>
</tr>
<tr>
<td>0.25:00</td>
<td>90.00</td>
<td>-</td>
<td>90.70</td>
<td>90.00</td>
<td>76.74</td>
<td>80.26</td>
<td>85.47</td>
<td>80.65</td>
<td>Fail</td>
</tr>
</tbody>
</table>
Online HPLC System for automated Tablet Dissolution Testing

A Graphical display of Specification Compliance is illustrated above.

**Data for Different Groups can be Displayed with Individual Statistics…**

When data for analysis with multiple groups are displayed, the groups are displayed separately as though they are dissimilar tests, each with their own statistics. This allows analysis of the quality of the data from each group without having to export data into Excel, for example.

**First Group of Samples with their statistics**

<table>
<thead>
<tr>
<th>Time (Minutes)</th>
<th>Sample 1</th>
<th>Sample 2</th>
<th>Sample 3</th>
<th>Mean</th>
<th>Sample 4</th>
<th>Sample 5</th>
<th>Sample 6</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>00:00:00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>00:15:00</td>
<td>7.72</td>
<td>6.95</td>
<td>2.25</td>
<td>6.31</td>
<td>1.02</td>
<td>7.72</td>
<td>10.61</td>
<td>11.50</td>
<td>10.04</td>
</tr>
<tr>
<td>00:30:00</td>
<td>17.37</td>
<td>16.60</td>
<td>25.10</td>
<td>19.65</td>
<td>4.70</td>
<td>27.41</td>
<td>15.15</td>
<td>13.51</td>
<td>18.69</td>
</tr>
<tr>
<td>00:45:00</td>
<td>35.81</td>
<td>41.70</td>
<td>42.06</td>
<td>41.06</td>
<td>2.20</td>
<td>38.01</td>
<td>41.70</td>
<td>38.61</td>
<td>39.64</td>
</tr>
<tr>
<td>01:00:00</td>
<td>52.12</td>
<td>52.51</td>
<td>52.51</td>
<td>52.36</td>
<td>0.22</td>
<td>54.44</td>
<td>52.51</td>
<td>57.14</td>
<td>54.70</td>
</tr>
<tr>
<td>01:15:00</td>
<td>60.62</td>
<td>60.23</td>
<td>64.48</td>
<td>61.78</td>
<td>2.35</td>
<td>61.00</td>
<td>61.78</td>
<td>63.32</td>
<td>62.03</td>
</tr>
<tr>
<td>01:30:00</td>
<td>68.73</td>
<td>72.20</td>
<td>74.13</td>
<td>71.68</td>
<td>2.74</td>
<td>70.86</td>
<td>60.62</td>
<td>66.41</td>
<td>65.89</td>
</tr>
<tr>
<td>01:45:00</td>
<td>77.22</td>
<td>60.31</td>
<td>78.38</td>
<td>78.64</td>
<td>1.56</td>
<td>77.22</td>
<td>71.81</td>
<td>75.29</td>
<td>74.77</td>
</tr>
</tbody>
</table>

**Second Group of Samples with their statistics**

<table>
<thead>
<tr>
<th>Time (Minutes)</th>
<th>Sample 1</th>
<th>Sample 2</th>
<th>Sample 3</th>
<th>Mean</th>
<th>Sample 4</th>
<th>Sample 5</th>
<th>Sample 6</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>02:00:00</td>
<td>95.33</td>
<td>84.17</td>
<td>82.24</td>
<td>83.91</td>
<td>1.56</td>
<td>91.47</td>
<td>78.15</td>
<td>80.69</td>
<td>82.64</td>
</tr>
<tr>
<td>02:15:00</td>
<td>85.18</td>
<td>88.03</td>
<td>84.94</td>
<td>87.39</td>
<td>2.20</td>
<td>88.32</td>
<td>82.40</td>
<td>89.95</td>
<td>87.13</td>
</tr>
<tr>
<td>02:30:00</td>
<td>100.39</td>
<td>96.53</td>
<td>88.42</td>
<td>95.11</td>
<td>6.11</td>
<td>96.91</td>
<td>91.86</td>
<td>100.00</td>
<td>95.27</td>
</tr>
<tr>
<td>02:45:00</td>
<td>100.39</td>
<td>100.39</td>
<td>85.33</td>
<td>95.37</td>
<td>8.68</td>
<td>96.91</td>
<td>91.12</td>
<td>99.61</td>
<td>95.89</td>
</tr>
<tr>
<td>03:00:00</td>
<td>100.39</td>
<td>95.76</td>
<td>88.19</td>
<td>95.11</td>
<td>5.63</td>
<td>96.91</td>
<td>91.86</td>
<td>100.39</td>
<td>96.40</td>
</tr>
</tbody>
</table>
Monitoring pH and Dissolution Data Simultaneously…

This is particularly useful for enteric coated formulations where the dissolution profile is followed as a function of changing pH.

During the experiment for pH change methods, readings are taken at multiple time points and WinDiss32-V3 displays and monitors Absorbance, pH, Temperature and Speed as well as calculating the %Dissolution in real time; pH probes may be placed in either one vessel or may be placed in all active vessels via the MES8 Micro Electrode Selector. Graphs can be displayed simultaneously for all data types (pH, Absorbance, %Dissolved etc) during and after the analysis is completed.

Graph showing a pH profile obtained from monitoring the pH in a method with a 3 fold medium change

Corresponding % Dissolved Data Graph

Dynamic Report Editor…

The WinDiss32-V3 integrated solutions report organiser allows users to produce customised reports with the required information by selecting from a combination of objects such as Method Header, Data tables, Method parameters, Graphs and the company logo.

These details include method parameters as well as any data captured during the test such as Bath Temperature, Paddle Speed, Time Intervals as well as Absorbance, Concentration and % Dissolved.

FDA 21 CRF part 11 Compliance…

Administration management allows the system administrator to configure WinDiss32-V3 integrated solutions to meet one of the fullest implementation of 21 CFR Part 11 compliance of any data management system available today.

Individual access to the system is by a unique user name and password, configured for each user with Group or individual access rights, and the users full name is displayed when the user logs on successfully and on all documentation generated by the system for the user.
Configurable Centralised Security

Functionality is provided to allow the administrator to set limits to control the security of the network environment for WinDiss32 integrated solution workstations.

The system administrator can manage password expiry and Re-use, Log Off Times and text to instruct users in their local language what to do in case of access failure, etc.

These activities can be performed remotely from any WinDiss32-V3 integrated solutions networked workstation and only ever need to be performed once for each user.

With other systems that are not networked, this procedure would have to be repeated for each workstation.

Signing and Tracking Signature on Records...

WinDiss32-V3 integrated solutions provide total management for signing, from start to finish. Configuring the number of signing levels, the Users for each level, Signer Activity and Meaning are all managed by the company's administrator.

The administrator can use up to 5 signature levels appropriate to the structure of the company. These levels can be for Analysts, Supervisors and Qualified personnel.
Once the analysis is completed the signing of records can be performed. For HPLC analysis with certain Chromatography Data Systems, no signing can be performed until the records on the CDS are signed.

Records will only be displayed automatically for the Groups that the user is allowed to log on to and has the rights to sign for. Further filtering of records, to limit the number displayed, is provided using the Signing Query dialogue shown here.

Once data is acquired in a Group configured for signing, a summary of records to be signed can be obtained and records for signing are clearly visible in dark blue with red indicating the signing for other levels as shown below.

Single or multiple record(s) can be signed in any one session.
The signing process is very simple, clear and precise, the User must view the records selected (which they have access to sign) before the User can sign these records.

Once the records are eligible for signing, Signer Action and Meaning are selected from a list of predefined Actions and Meaning then the user name and password are required to complete signing.

Once records are signed, the signing is clearly shown on the footer of each page, as they would appear for manual conventional signatures.

Non-Editable Graphic Electronic Records...

WinDiss32-V3 integrated solutions is supplied with the WinDiss32-V3 Graphics Printer that provides compliance with 21 CFR Part 11 requirements for “human readable form”.

These reports can be circulated, emailed etc., in the safe knowledge that they are non-editable.

The Graphics Printer can capture any WinDiss32-V3 integrated solutions report into TIF, BMP or JPG (JPEG) and save them as electronic files.

The TIF format can save a multiple page report and the Image Viewer supplied automatically displays the printed file image for verification.

User Queryable Audit Trail and Record History...

WinDiss32-V3 integrated solutions Audit Trail lists all user activity that creates, deletes or modifies; i.e., from logging on and off to editing of method and data records. This Audit Trail can have filters to limit the volume of information from a search. The results from any search can be printed.
Networking...

WinDiss32-V3 integrated solutions uses **Oracle Database 10g** for data storage and management. With Oracle your information is always available and secure. Oracle is the best choice for large enterprises, small and midsize businesses, and departments alike. **Oracle Database 10g** has unique security features that address privacy, regulatory compliance, and data consolidation requirements.

Oracle automates time-consuming, error-prone administrative tasks, so DBAs can focus on strategic business objectives with superior manageability and significant cost savings over conventional databases.

The Oracle network database provides a central relational database that contains records from WinDiss32-V3 integrated solutions workstations. Results are accessible from any workstation on the company’s network linked to our Oracle database.

Each WinDiss32-V3 integrated solutions system runs from a workstation PC, each hardware configuration can be unique.

With this configuration, records can be signed remotely from any WinDiss32-V3 integrated solutions client. For example, it is now possible for analysts and supervisors or managers to view, sign, print etc away from the laboratory area.